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TRIBROMETHANOL ANESTHESIA*

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Of the anesthetic agents recently introduced into clinical practice, tribromethanol appears to be one of the most promising. The drug was first introduced in Germany nearly three years ago, and there are now from 300,000 to 400,000 cases in which it has been used. In spite of this fairly wide experience with it in Europe, there is still a great difference of opinion among clinicians regarding its usefulness. Because of this situation, we have attempted to gather together the available pharmacologic and clinical data, to verify a few points by experimentation on animals and, with the knowledge so obtained, to apply the anesthetic to the human being.

REVIEW OF THE LITERATURE

CHEMICAL AND PHYSICAL PROPERTIES

Tribromethanol was first prepared, in 1923, by Willstätter and Duisberg[1] through the reduction of bromal hydrate in yeast-sugar fermentation. In the manufacture of the substance on a commercial scale, this method of preparation apparently has been replaced by a purely chemical synthesis. The latter process is based on the reduction of bromal hydrate by alcohol in the presence of aluminum ethoxide as a catalyst.[2] The pure drug consists of colorless monoclinic prisms, which are odorless and which melt at 80 C. According to Eichholtz,[3] it dissolves without decomposition in water heated to 45 C., but in water heated to about 70 C., the dissolved drug slowly hydrolyzes with the formation of hydrobromic acid and dibromacetaldehyde. On steam distillation of a solution of it, it is readily volatile. The solution of the pure drug in distilled water is neutral to congo red, but if heated to the point of hydrolysis, it becomes distinctly acid to this indicator. It is therefore recommended that solutions of the anesthetic be made

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1. Willstätter, R., and Duisberg, W.: Zur Kenntnis des Trichlor- und Tribromäthyl-Alkohols, Ber. d. deutsch. chem. Gesellsch. **56**:2283, 1923.

2. British patent no. 235,584, June 12, 1924.

3. Eichholtz, F.: Ueber rektale Narkose mit Avertin (E 107) Pharmakologischer Teil, Deutsche med. Wchnschr. **53**:710, 1927.

at a temperature not in excess of 45 C., and that they be tested with 0.1 per cent solution of congo red prior to instillation into the rectum, in order to avoid intestinal irritation resulting from the acid products of hydrolysis. When an aqueous solution of tribromethanol is permitted to stand for several days at room temperature, some decomposition takes place. For this reason, it has been recommended that solutions for rectal anesthesia be prepared less than twelve hours before use. Blomfield and Shipway [4] showed that 3 per cent solutions kept in the dark at room temperature remain neutral to congo red for about forty-eight hours. They quote other English workers who found no decomposition in a 3 per cent solution kept at room temperature for fourteen days, while Parsons [5] claimed to have kept solutions exposed to light and air for as long as three months without evidence of decomposition. Blomfield and Shipway observed that exposure of the solution to ultraviolet light produced rapid hydrolysis. The drug dissolves readily in alcohol, ether, ethyl acetate, chloroform, acetone, petrolic ether and similar organic solvents. It may be distilled in a high vacuum without decomposition; its boiling point at 11 mm. pressure is 93 C.[1]

PHARMACOLOGIC ACTION

Dosage.—Experiments by Eichholtz [3] indicate that the response of different species of animals used in ordinary laboratory experimentation varies over a considerable range. Thus, in cats, anesthesia is obtained following the oral administration of 0.15 Gm. per kilogram of weight. Mice and rabbits, on the other hand, require oral doses as high as from 0.5 to 1.6 Gm. per kilogram of body weight in order that anesthesia may be produced. Administration by rectum produces similar variations: Mice require only from 0.08 to 0.15 Gm. per kilogram for the production of deep anesthesia, whereas dogs require 0.15 Gm. per kilogram. When administered by rectal injection, the minimum lethal dose for experimental animals is from 75 to 100 per cent in excess of the anesthetic dose. Eichholtz tested the possibility of chronic poisoning from repeated injection of the drug by giving daily rectal doses of from 0.4 to 0.5 Gm. per kilogram to white mice over a period of seven weeks. No tolerance to the drug was observed, and a pathologic examination of the tissues of these animals revealed no lesions. Induction of anesthesia in animals following rectal administration is rapid; the rate of recovery of rabbits from such anesthesia is said to be twice as rapid as that from chloroform

4. Blomfield, J., and Shipway, F. E.: The Use of Avertin for Anesthesia, Lancet **1**:546, 1929.

5. Parsons, F. B.: Some Pharmacological Aspects of Avertin, Brit. M. J. **2**:709, 1929.

anesthesia and as fast as recovery from ether. Lendle [6] found that fasting animals were more susceptible to the effect of the anesthetic.

Absorption.—Straub [7] studied the rate of absorption of the drug from the intestinal tract in three human beings in whom tribromethanol was used as a rectal anesthetic. They were persons of varying susceptibility to the drug and were studied in order to determine whether or not resistance to or susceptibility to the drug was reflected in the rate of its absorption from the intestine. His results indicated that so far as rate of absorption is concerned, there is no difference between the susceptible and the resistant subject. The drug was shown to have been almost quantitatively absorbed within a period of two hours following its administration.

Sebening [8] showed that the concentration of the drug in the blood stream rises to a maximum of 9 mg. per hundred cubic centimeters twenty minutes after the rectal administration of the anesthetic solution. This concentration falls rapidly to 3 mg. per hundred cubic centimeters, and then slowly to 0.15 mg. per hundred cubic centimeters, a concentration at which awakening takes place.

That the rate of absorption of the drug from the intestine varies considerably during an anesthesia of two and one-half hours' duration is demonstrated by one of Straub's experiments. This showed that during the first seventeen minutes following rectal administration of the drug in 3 per cent solution, the tribromethanol was absorbed at the rate of 0.47 Gm. per minute, and water was absorbed at the rate of 14.6 Gm. per minute. Three further rectal injections of the drug made at subsequent intervals of from approximately one-half to one hour indicated that the rate of absorption of the drug through the intestinal wall had fallen to a value of from 0.04 to 0.08 Gm. per minute, while the rate of absorption of water had fallen to a value of from 1 to 2 Gm. per minute. This experiment shows clearly that the permeability of the intestinal wall decreases following the first rectal injection of tribromethanol.

Excretion.—Endoh [9] demonstrated that tribromethanol is excreted in the urine of dogs and rabbits in conjugation with glycuronic acid. This was confirmed by Straub [10] in his study of the excretion of the

6. Lendle, L.: Experimentelle Untersuchungen über die Dosierung und die Elimination des Avertins, Narkose u. Anaesth. **1**:239, 1928.

7. Straub, W.: Rektalnarkose mit Avertin (Resorption und Dosierung), München. med. Wchnschr. **75**: 593, 1928.

8. Sebening, W.: Report of 52nd Annual Meeting of German Surgical Society, Berlin, April 11-14, 1928, Zentralbl. f. Chir. **55**:1360, 1928.

9. Endoh, C.: Ueber das Verhalten des Tribromäthyl-Alkohols im Tierkorper, Biochem. Ztschr. **152**:276, 1924.

10. Straub, W.: Rektalnarkose mit Avertin: II. Ausscheidung und Nebenwirkungen, München. med. Wchnschr. **75**:1279, 1928.

drug following rectal administration of it to the human being in anesthetic doses. He showed that no bromine was eliminated in the feces or perspiration. He likewise showed that no bromine was excreted in the urine in the form of bromide, which indicated that the drug was not hydrolyzed in the body. Chemical analyses of the urine of patients receiving the drug as a rectal anesthetic showed that the concentration of the drug in the urine increased rapidly to a maximum at four hours following the administration, and then diminished moderately during the following ten hours. Only a small amount was eliminated in the urine during the second twenty-four hours. Chemical analyses showed that the drug was excreted quantitively in the urine during the forty-eight hour period following its administration.[11] The somewhat qualitative observations of Nestmann[12] are essentially in agreement with Straub's results. More recent work by Parsons[5] showed that rabbits receiving subcutaneous doses of 0.4 Gm. per kilogram eliminated from 54 to 73 per cent of the drug in the urine during the first twenty-four hours, and practically all of the drug was eliminated by the end of three days. In the case of one human being, 66 per cent was excreted in the urine in the first twenty-four hours and 91 per cent was excreted in six days.

Effect on Circulation.—Straub[10] also studied the effect of the drug on the heart, since from its chemical similarity to chloroform and chloral hydrate, one might expect to find impairment of the heart's function. Blood containing 0.12 Gm. of tribromethanol per hundred cubic centimeters gave no alteration in either the strength or the stroke volume of the heart, and paralysis was observed only at much greater concentrations. The moderate fall in arterial blood pressure observed in anesthesia due to tribromethanol probably results from vasomotor depression. However, Parsons[5] found that on perfusion of the isolated heart of the rabbit with tribromethanol in Ringer's solution, concentrations of 1:5,000 and 1:2,500 had definite depressing effects, while a concentration of 1:1,250 caused systolic standstill in five minutes. Killian,[13] Unger and May[14] and Domrich[15] studied the action of an anesthetic dose of tribromethanol on the heart, using the electrocardiographic method. They all reached the same conclusion, that with the ordinary anesthetic dose

11. Straub, W.: Klinisches und pharmakologisches zur Avertin Narkose, Klin. Wchnschr. **7**:2346, 1928.

12. Nestmann, F.: Klinisches und pharmakologisches zur Avertin Narkose, Klin. Wchnschr. **7**:1901, 1928.

13. Killian, H.: Zur pharmakologischen Wirkung von E-107, Zentralbl. f. Chir. **54**:1997, 1927.

14. Unger, E., and May, H.: Elektrocardiographische Untersuchungen während der Narkose (insbesondere Avertin-narkose), Zentralbl. f. Chir. **54**:3272, 1927.

15. Domrich: Zur Wirkung des Avertins auf den Kreislauf, Zentralbl. f. Chir. **55**:2632, 1928.

there is no appreciable change in the conduction mechanism. Franken and Schürmeyer [16] found that the volume of circulating blood was diminished as much as from 20 to 25 per cent during anesthesia following rectal injection of the drug in man.

Effect on Respiration.—Experiments in the rabbit [10] showed that following the rectal administration of an anesthetic dose of tribromethanol, there is a decided diminution in both the respiratory rate and the minute volume. These reach a minimum value about ten minutes after the instillation of the drug and then gradually return toward the normal values. Under similar circumstances, Eichholtz [8] found that although the respiratory rate was markedly decreased during the anesthesia, the minute volume remained essentially the same. There is also considerable difference of opinion regarding the response of the respiratory center to stimulation by carbon dioxide during anesthesia due to tribromethanol. In experiments on animals, Killian [17] produced results that he interprets as demonstrating a decrease in sensitivity of the respiratory center to carbon dioxide as a result of the anesthesia. However, these experiments show that while there may be a decrease in the response of the respiratory center, as it becomes progressively more depressed, as long as the center is functional there is a definite stimulating effect produced by the inhalation of carbon dioxide. This agrees with the clinical results reported by Polano,[18] Martin [19] and Flörcken,[20] who have used carbon dioxide successfully as a stimulant in cases of respiratory embarrassment during tribromethanol anesthesia. Neither Straub [10] nor Bender [21] was able to elicit respiratory stimulation by the injection of lobeline into animals in which the respiration was impaired by the anesthetic agent.

Margin of Safety.—Kärber and Lendle [22] showed that surgical anesthesia may be obtained in rabbits from the rectal administration of 0.35 Gm. per kilogram, whereas the average fatal dose of the drug administered by rectum is 0.55 Gm. per kilogram. Thus it appears that

16. Franken, H., and Schürmeyer, A.: Kollaps und Narkose, Narkose u. Anaesth. **1**:437, 1928.

17. Killian, H.: Weitere experimentelle Erfahrungen mit Avertin, Narkose u. Anaesth. **1**:119, 1928; footnote 13.

18. Polano, O.: Die Rektalnarkose mit E-107 bei gynäkologischen Untersuchungen und Operationen, München. med. Wchnschr. **74**:630, 1927.

19. Martin, B.: Unsere heutige Kenntnis des Avertin und seine praktische Verwendung, Deutsche med. Wchnschr. **54**: 2068 and 2110, 1928.

20. Flörcken, H.: Beeinflussung des Avertinschlafs durch Kohlensäureinhalation, Zentralbl. f. Chir. **55**:1925, 1928.

21. Bender, K. W.: Klinische und tierexperimentelle Studien über die Avertinnarkose, Beitr. z. klin. Chir. **143**:599, 1928.

22. Kärber, G., and Lendle, L.: Untersuchungen über kombinierte Narkosen, Arch. f. exper. Path. u. Pharmakol. **143**:88, 1929.

surgical anesthesia requires 64 per cent of the fatal dose. This is in line with experience with other general anesthetic agents, the dose of which for surgical anesthesia is believed to represent approximately from two-thirds to three-fourths the fatal amount.

Effect on Blood Chemistry.—A study of the acid-base equilibrium during anesthesia from tribromethanol by Wymer and Fuss [23] showed that this drug more closely resembles chloroform than ether in its tendency to produce acidosis in experimental animals. During anesthesia in the human being, the hydrogen ion concentration of the blood was found to remain practically normal. The blood sugar rose sharply, but returned to the normal range in from six to twenty-four hours after the induction of the anesthesia. The alkali reserve was not materially altered.

Experiments by Stiasny [24] showed that the calcium content of the blood serum is decreased from 7 to 13 per cent during anesthesia produced by tribromethanol. In this respect, tribromethanol is similar to ether.

CLINICAL APPLICATION

Since tribromethanol has been used by numerous European clinicians in obtaining general anesthesia in cases numbering to hundreds of thousands, it is difficult to make a complete résumé of all the various technics employed. The excellent review of Killian,[25] the reports of Anschütz [26] and of Blomfield and Shipway,[4] the two questionnaires of Schwalbe [27] and the symposiums of the German surgical societies provide a simple method for obtaining a fair approximation of previous experience with this new type of rectal anesthesia. A more recent report by Guttman [28] gives a résumé of the recent experiences of German workers. For detailed data, the original literature must be consulted.

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23. Wymer, I., and Fuss, H.: Die Säurebasenverhältnisse bei der Avertinnarkose, zugleich ein Beitrag zur pathologischen Physiologie der Avertinnarkose, Deutsche Ztschr. f. Chir. **211**:281, 1928; Eine vergleichende Studie über die Säurebasenverhältnisse bei der Äther-Chloroform und Avertinnarkose, Narkose u. Anaesth. **1**:283, 1928.

24. Stiasny, H.: Ueber Narkose mit Avertin (E-107) und ihren Einfluss auf den Serumkalziumspiegel beim Hunde, Tierärztl. Rundschau **33**:871, 1927.

25. Killian, H.: Die bisherigen Ergebnisse mit der Avertinrektalnarkose, Narkose u. Anaesth. **1**:16, 1928; Avertin-Rectal Anesthesia: The Results to Date, Brit. J. Anesth. **5**:168, 1928; **6**:48, 1928.

26. Anschütz, W.: Zur Eröffnung einer allgemeinen Aussprache über die Avertinnarkose, Zentralbl. f. Chir. **55**:2371, 1928.

27. Schwalbe, J.: Der gegenwärtige Stand der Avertinnarkose: Eine Umfrage, Deutsche med. Wchnschr. **53**:2064, 1927; Ueber die Avertinnarkose: 2 Umfrage, ibid. **54**:558, 1928.

28. Guttman, J. R.: Rectal Anesthesia with Tribromethylalcohol, Ann. Surg. **90**:407, 1929.

Preanesthetic Medication.—The general plan of the preanesthetic technic employed by most of the German workers is uniform. The intestinal tract is emptied by an enema or mild cathartic the evening before the operation, and the patient is placed on a liquid died. Barbital is also given the evening before. The morning of the operation a hypodermic injection of pantopon, morphine, scopolamine or narcophine is given about one and one-half hours prior to the administration of tribromethanol. There is a wide variation of opinion regarding the advisability of giving such preanesthetic narcotics. Although Kreuter [29] reported better anesthesia without these narcotics, the majority of the clinicians use one or more of these drugs, administered by hypodermic injection.

Preparation of Solution.—Tribromethanol is usually administered in 3 per cent solution in distilled water at body temperature. In order to hasten solution, the crystalline drug is dissolved in warm water at temperatures not to exceed 45 C. A few clinicians recommend temperatures not in excess of 60 C. Because of hydrolysis, solutions are not used more than twelve hours after their preparation. It is customary to test the solution with congo red just prior to its administration. Any solution giving an acid reaction must be discarded.

Although most surgical clinics use tribromethanol in 3 per cent solution, a few have found it advisable to work with lower concentrations. Glaesmer and Amersbach [30] varied the concentration of the drug between the limits of 2 per cent and 3 per cent depending on the age of the patient. In aged patients, low concentrations and low dosages are employed, whereas in youthful patients a higher concentration is utilized. Martin [19] reported good results with 2.5 per cent solution of the drug, but no advantage appears to obtain from the employment of the more dilute solution.[31]

In place of distilled water, some workers [32] recommended physiologic solution of sodium chloride as a solvent for the drug. Nordmann [33] seemed to have difficulty with intestinal irritation following the use of aqueous solutions. The use of 1 per cent salep mucilage as a solvent was found to obviate this difficulty. Other workers use milk as a solvent.

29. Kreuter, E.: Sechshundertfünfzig Rektalnarkosen mit Avertin (E 107), Zentralbl. f. Chir. **54**:3074, 1927.

30. Glaesmer, E., and Amersbach, R.: Zur Kritik der Avertinnarkose, München. med. Wchnschr. **74**:1835, 1927.

31. Butzengeiger, O.: Zur Avertin Aussprache, Zentralbl. f. Chir. **56**:204, 1929.

32. Melzner, E.: Zur Beurteilung der Rectalnarkose mit E 107 (Avertin), Arch. f. klin. Chir. **148**:698, 1927. Lobenhoffer, W.: Ueber Narkosen mit E 107, München. med. Wchnschr. **74**:849, 1927.

33. Nordmann, O.: Die Rektalnarkose mit E 107, Zentralbl. f. Chir. **54**:1055, 1927.

The majority of German clinicians report little difficulty from intestinal irritation when neutral aqueous solutions are used.

A recent modification by Schulze [34] is the use of a solution of tribromethanol in amylene hydrate (tertiary amyl alcohol). A solution may be obtained, 1 cc. of which will contain 1 Gm. of tribromethanol and 0.5 Gm. of amylene hydrate. Apparently this solution is comparatively stable. Amylene hydrate is said to be not only a good solvent for the drug, but the ease of volumetric measurement of such a solution avoids the necessity of weighing out the drug. One may simply measure out the requisite dose of drug with a pipet and add the necessary amount of water at body temperature. Amylene hydrate exerts a mild narcotic effect of its own, and is said to have a stimulating effect on the respiratory center which partially offsets the depressing effect of the tribromethanol.

Dosage.—The dosage of tribromethanol employed by German workers in producing general anesthesia has varied from 0.08 Gm. per kilogram to over 0.2 Gm. per kilogram. The first American workers to report on the use of tribromethanol as a rectally administered anesthetic were Honan and Spiegel.[35] They recommended dosages of from 0.1 to 0.15 Gm. per kilogram of body weight, although in the cases that they reported the patients were all treated with from 0.15 to 0.175 Gm per kilogram of body weight. Few clinicians exceed 0.15 Gm. per kilogram, and the general trend seems to be toward a dosage of 0.125 Gm. per kilogram or less. Most of the deaths reported during tribromethanol anesthesia have followed the administration of doses of 0.15 Gm. or more per kilogram of body weight. According to Nordmann,[33] the dose recommended by the manufacturer of the drug is 0.1 Gm. per kilogram. Köller [36] came to the conclusion that 0.15 Gm. per kilogram is too high a dose in a case of pulmonary involvement. Butzengeiger [37] used a scheme of fractional dosage that appears to have worked out satisfactorily. The method is to give a basal dose of 0.1 Gm. per kilogram. If sleep has not supervened in from five to seven minutes, a further injection of 0.025 Gm. per kilogram is given. If this still fails to produce surgical anesthesia in another ten or fifteen minutes, a final injection of 0.025 Gm. per kilogram is given. This makes a total of 0.15 Gm. per kilogram, which he does not recommend exceeding. If necessary, deeper anesthesia is obtained by

34. Schulze, W.: Ueber Rektalnarkosen mit Avertin-Amylenhydratlösung, Deutsche med. Wchnschr. **54**:1928, 1928.

35. Honan, W. F., and Spiegel, A.: Colonic Anesthesia with Avertin, J. A. Inst. Homœop. **22**:7, 1929.

36. Köller, T.: Avertinnarkose bei Phrenicusexairese, Zentralbl. f. Chir. **55**: 2498, 1928.

37. Butzengeiger, O.: Klinische Erfahrungen mit Avertin (E 107), Deutsche med. Wchnschr. **53**:712, 1927; footnote 31.

supplementary inhalation of ether. Schulze [34] uses a similar method, but employs 0.125 Gm. per kilogram as the usual basal dose for adults, and 0.15 Gm. per kilogram for children. In either case, only one additional injection of 0.025 Gm. per kilogram is made, if the desired grade of anesthesia is not obtained.

The obvious trend of European technic in producing anesthesia with tribromethanol is toward a more conservative scheme of dosage. This is accomplished by administering a basal dose followed by a succeeding dose if needed, or by supplementing the basal tribromethanol anesthesia by means of inhalation or local anesthesia. The latter method is advocated by the English clinicians.[4]

Depth and Duration of Anesthesia.—The depth and duration of the anesthesia following rectal administration of tribromethanol vary widely in different persons. Although Roith [38] was unable to observe any variation of susceptibility in patients of different ages, most workers report a decreased response of children to the anesthetic. Schulze [34] found that while only 30 per cent of children (from 1 to 10 years of age) were completely anesthetized by the drug, from 55 per cent to 75 per cent of older subjects (from 10 to 70 years of age) were completely anesthetized by a similar dose. Statistics given by Roith,[38] Kreuter,[29] Conrad [39] and Lobenhoffer [40] indicate that at single doses of from 0.12 to 0.15 Gm. per kilogram, about 60 per cent of all patients give complete surgical anesthesia. In from 15 per cent to 30 per cent, a small amount of accessory anesthetic (ether, ethyl chloride, acetylene, ethylene or methylene chloride, but not chloroform) was required for securing the necessary depth of narcosis. A similar percentage required a moderate amount of accessory anesthetic, but only from 3 to 10 per cent required considerable quantities of additional anesthetic.

According to European clinicians, blood pressure under tribromethanol anesthesia usually either remains unchanged or falls slightly (from 10 to 30 mm. mercury). Respiration is not greatly affected. The pupils are constricted. A characteristic flushing of the face has been noted. The body temperature falls slightly. Cyanosis is said to be comparatively rare.

In the European clinics, administration of the solution is accomplished by means of a small rubber catheter and syringe. The catheter is usually inserted into the rectum to a depth not in excess of 20 cm. Lobenhoffer [40] devised a rectal tube fitted with a rubber balloon, which is separately inflated so as to prevent leakage of the anesthetic solution.

38. Roith, O.: Zur Avertinnarkose, München. med. Wchnschr. **75**:598, 1928.

39. Conrad, G.: Klinische Erfahrungen über die Rektalnarkose mit Avertin (E 107) bei gynäkologischen und geburtshilflichen Operationen, Zentralbl. f. Gynäk. **51**:2222, 1927.

40. Lobenhoffer (footnote 32, second reference).

According to the German clinicians, one of the most desirable features about tribromethanol anesthesia is the ease of its induction and of recovery from it and the comparative freedom from nausea and vomiting. Following the administration of the anesthetic, the patient becomes more and more drowsy and in about seven minutes has fallen into a deep sleep. In from fifteen to twenty minutes, anesthesia has reached the depth required for operation. The duration of deep anesthesia varies considerably over a range of from one to six hours, depending on the person and the dose. This is followed by gradual awakening. There is no period of excitement during either the induction or the recovery. Nausea and vomiting are said to be extremely rare, except in cases in which considerable ether has been used as an additional anesthetic. The patient has no recollection of anything that has taken place during the latter period of the induction or during the operative procedure. Levy-Dorn [41] considered these desirable aspects of tribromethanol anesthesia to be of great importance in the justification of its clinical use.

Dangers and Remedies.—The chief dangers encountered in the use of tribromethanol for the production of anesthesia (aside from the use of overheated, hydrolyzed solutions and overdosage) appear to be incidental to excessive depression of the respiration and circulatory mechanism and impairment of the secretory organs through which the drug is detoxified. Embarrassment of respiration and heart was successfully handled by Melzner [32] by the intravenous injection of caffeine and epinephrine or by washing out the intestine with a caffeine solution. The antitotal action of caffeine injected intravenously was demonstrated in animals by Herzberg.[42] Such injections were found to have a marked effect in shortening the duration of narcosis, as well as in decreasing its depth. He was unable to protect animals against the ordinarily fatal dose of tribromethanol by means of the injection of caffeine, however. There apparently is a difference of opinion as to the value of ephedrine in combating circulatory depression during tribromethanol anesthesia. Schmidt [43] reported beneficial effects and recommended it as a prophylactic agent, while Schrank [44] found it to be of no value. As has been pointed out earlier in this discussion, several clinicians found carbon

41. Levy-Dorn, M.: Vergleich zwischen Aether- und Rektal-narkose mit E 107 (Avertin), Med. Klin. **23**:871, 1927.

42. Herzberg, M. H.: Pharmakologische Versuche mit Avertin, Deutsche med. Wchnschr. **54**:1044, 1928.

43. Schmidt, H.: Das Ephedrin in der operativen Praxis, Zentralbl. f. Chir. **55**:3207, 1928.

44. Schrank, H.: Avertin und Kreislauf, Zentralbl. f. Chir. **55**:3205, 1928.

dioxide to be of no value in stimulating respiration during the anesthesia. The efficacy of lobeline as a respiratory stimulant does not seem to have been satisfactorily established. Tribromethanol for the production of anesthesia is said to be contraindicated in cases of damaged kidneys and liver, serious hypertension and cachexia. In addition to its use in general surgery, the anesthetic has found application in psychiatry in the handling of excited patients.[45] Its use in childbirth does not seem to have met with such great success.[46] Läwen [47] found it to be of value in the treatment for tetanus.

Deaths that are fairly attributable to reasonably conservative doses of tribromethanol are comparatively rare. Glaesmer and Amersbach [30] cited records of 13 deaths in 3,000 anesthesias. They further analyzed these 13 fatal instances and showed that, in general, the deaths were in connection with the use of hydrolyzed anesthetic solution, overdosage or a poor grade of surgical risk. Similar estimates of the mortality from the use of tribromethanol for the production of anesthesia have been made by Kotzoglu [48] and by Konig.[49] A later estimate of the mortality in tribromethanol anesthesia is 1 in 7,500.[50]

PHARMACOLOGIC STUDIES OF TRIBROMETHANOL

The first preparation of tribromethanol used was supplied by Dr. Helmut Schmidt of the Hamburg-Eppendorf Hospital, Germany. A further supply was provided by the Winthrop Chemical Company. It was a white, crystalline powder melting sharply at from 79.5 to 80 C. Chemical analysis by the Carius method showed the product to contain 84.9 per cent bromine, which corresponds favorably with the theoretical value of 84.8 per cent for tribromethanol.

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45. Blume, G.: Ueber Avertin in der Psychiatrie, Deutsche med. Wchnschr. **53**:1307, 1927. Enke, W., and Westphal, K.: Avertin als Hypnotikum und Dauerschlafmittel in der Psychiatrie, Ztschr. f. d. ges. Neurol. u. Psychiat. **114**:616, 1928.

46. Martin, E.: Avertin in der Geburtshilfe, Monatschr. f. Geburtsh. u. Gynäk. **76**:241, 1927. Rodecourt, M.: Ueber Avertinnarkose bei gynäkologischen Operationen, Narkose u. Anaesth. **2**:39, 1929. Ujma, A.: Die Rektalnarkose bei gynäkologischen Operation, Narkose u. Anaesth. **1**:329, 1928. Mey, R.: Avertindämmerschlaf, Zentralbl. f. Gynäk. **52**:1127, 1928. Kienlin, H.: Bestrebungen zum Ausbau des geburtshilflichen Dämmerschlafes, Zentralbl. f. Gynäk. **52**:1946, 1928.

47. Läwen, A.: Weitere Erfahrungen über die symptomatische Behandlung des Tetanus mit Avertin, Zentralbl. f. Chir. **55**:194, 1928.

48. Kotzoglu, P.: Ueber die Todesfälle in Avertinnarkose, Zentralbl. f. Chir. **56**:2206, 1929.

49. Konig: Zentralbl. f. Chir. **56**:1895, 1929.

50. Proceedings of the Northwest German Surgical Society, Dec. 14-15, 1928 (Avertin Aussprache), Zentralbl. f. Chir. **56**:995, 1929.

PRELIMINARY ESTIMATIONS

Solubility.—Solutions of known concentration from 0.5 to 3 per cent of tribromethanol in distilled water were prepared and their refractive indexes determined at 40 C. by means of the immersion refractometer. From these data, the concentration of any solution in the range from 0 to 3.5 per cent tribromethanol could be calculated from its refractive index. Saturated solutions of tribromethanol in distilled water were prepared at room temperatures varying from 0 to 37 C., and the refractive indexes of such saturated solutions were determined at 40 C. The solubility of tribromethanol in this range of temperature is indicated in table 1. From table 1, it would be expected that a 3 per cent solution would deposit crystals of tribromethanol when cooling below 25 C.

TABLE 1.—*The Solubility of Tribromethanol at Temperatures from 0 to 37 C.*

Temperature, C.	Grams Tribromethanol per 100 Cc. Solution
0	1.90
9	2.15
26	3.05
37	3.70

TABLE 2.—*Results of Intraperitoneal Injection of Tribromethanol* in Rats*

Dosage, Gm. per Kg.	Results
0.50	Three animals died in fifteen minutes
0.45	Of three animals, two died within fifteen minutes
0.40	Of five animals, one died within fifteen minutes
0.35	Of eleven animals, one died in fifteen minutes, surgical anesthesia lasted from twenty to forty minutes
0.30	Light anesthesia lasted for from twenty to thirty minutes
0.20	Sleep lasted for nine minutes

* Three per cent aqueous solution of the crystals.

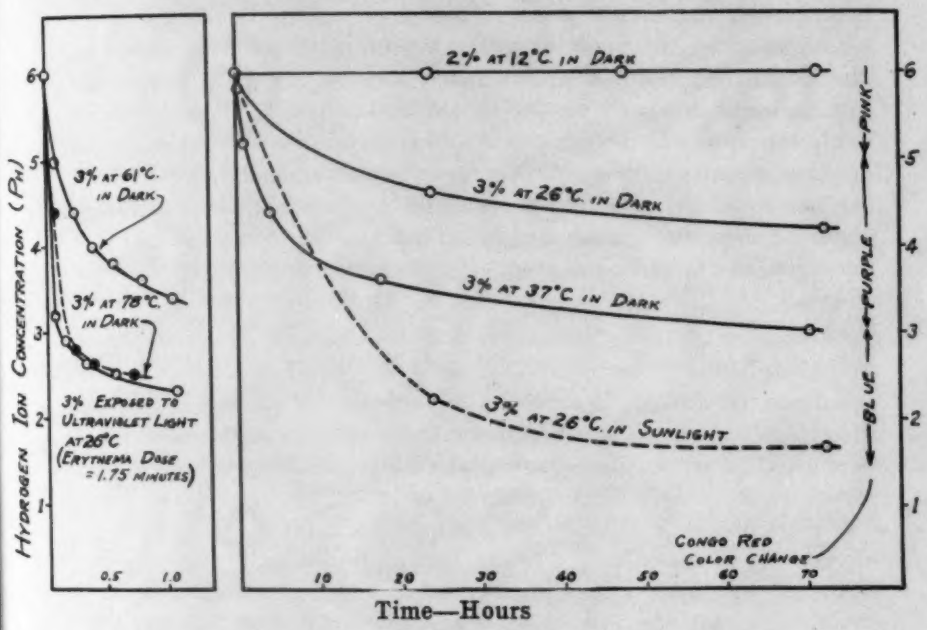
Stability toward Hydrolysis.—A study of the changes in the hydrogen ion concentration of tribromethanol solutions under varying conditions was made. The original solutions were prepared in the usual way by dissolving crystals of tribromethanol in ordinary distilled water at 40 C. Such solutions had the same hydrogen ion concentration as the water (from 5.8 to 6). The hydrogen ion concentration was determined by the colorimetric method, the indicator series of Clarke being used. The results are indicated in the accompanying chart.

TOXICITY AND EFFICIENCY IN EXPERIMENTAL ANIMALS

Rats.—Intraperitoneal injections of tribromethanol (3 per cent aqueous solution of the crystals) produced results as set forth in table 2. Rats given daily intraperitoneal doses of 0.3 Gm. per kilogram of body weight over a period of a week showed no evidence of cumulative action.

Tribromethanol in the soluble form (66 per cent by weight of tribromethanol and 34 per cent of tertiary amyl alcohol) was found to be slightly more toxic to rats than the crystalline form of the drug. The amyl alcohol apparently adds slightly to the toxicity of the preparation, since the average fatal dose was reduced from 0.45 to 0.37 Gm. per kilogram of body weight.

Rabbits.—The maximum oral dose which may safely be administered to rabbits is about 0.8 Gm. per kilogram of body weight (given in 3 per cent aqueous solution). This gives an anesthesia lasting from about


Hydrogen Ion Concentration (PH)
3% at 61°C. in Dark
3% at 78°C. in Dark
3% Exposed to Ultraviolet Light at 26°C (Erythema Dose = 1.75 minutes)
2% at 12°C. in Dark
3% at 26°C. in Dark
3% at 37°C. in Dark
3% at 26°C. in Sunlight
Congo Red Color Change
Pink
Purple
Blue
Time—Hours

Changes in the hydrogen ion concentration of solutions of tribromethanol under various conditions.

twenty to forty minutes. A moderately deep anesthesia, lasting from nine to twenty-four minutes, is obtained with 0.7 Gm. per kilogram, given orally. Lower doses produce sleep, but no anesthesia.

Intravenous doses of 3 per cent aqueous solution of tribromethanol produced a sudden but brief anesthesia. A slowly injected dose of 0.2 Gm. per kilogram of body weight was about the maximum that was tolerated. This produced anesthesia for approximately fifteen minutes. A dose of 0.15 Gm. per kilogram gave surgical anesthesia for only a few minutes, followed by a deep sleep of about ten minutes. Doses of 0.10 Gm. per kilogram produced only a deep sleep.

In order to ascertain the effect of tribromethanol on erythrocytes, rabbits' blood was added to solutions of the drug made up in physiologic solution of sodium chloride. At 37 C. complete hemolysis was observed within fifteen minutes in concentrations of 1.5 per cent and 2 per cent tribromethanol. One per cent solution produced partial hemolysis. Blood taken from rabbits that had received intravenous injections of 0.2 Gm. of tribromethanol per kilogram gave no evidence of hemolysis on centrifugation. Animals so anesthetized did not develop a hemoglobinuria. Any extensive hemolysis due to the low concentration of the injected drug seems improbable. Application of a 3 per cent aqueous solution of crystals of tribromethanol to the rabbit's cornea produced no apparent painful sensation, but gave rise to an anesthesia that was maintained for approximately twenty minutes. That slight irritation was produced was evidenced by the resulting congestion of the blood vessels of the eye. A 3 per cent solution of tribromethanol prepared from the fluid (67 per cent tribromethanol + 33 per cent amylene hydrate), when instilled into the conjunctival sac of a rabbit, produced somewhat greater congestion than the solution prepared from the crystalline form of the drug. No permanent harmful effects were observed.

Protection Against Toxic Effects of Cocaine and Procaine.—Since tribromethanol has been recommended as a basal narcotic for local anesthesia, particularly in ophthalmologic work, the question of its possible effect on the toxicity of local anesthetic agents was raised. Rabbits were given an ordinary anesthetic dose (oral), 0.7 Gm. of tribromethanol per kilogram of body weight, followed at once by a subcutaneous injection of cocaine hydrochloride. It was found that rabbits that ordinarily succumb to an injection of 100 mg. of cocaine hydrochloride per kilogram will withstand 300 mg. per kilogram under tribromethanol anesthesia. The ordinary fatal dose of procaine hydrochloride for rabbits is 800 mg. per kilogram. Under tribromethanol anesthesia, rabbits survived doses of 1.2 Gm. of procaine hydrochloride per kilogram. It is thus evident that tribromethanol anesthesia acts as a prophylactic agent against three times the ordinary fatal dose of cocaine hydrochloride, and 1.5 times the ordinary fatal dose of procaine hydrochloride.

Dogs.—In accordance with the recommended technic for producing anesthesia in man by rectal injection of tribromethanol, in dogs the administration of the anesthetic was preceded by a subcutaneous dose of morphine sulphate. This consisted of a total dose of from 30 to 45 mg. of morphine sulphate for each animal, administered about thirty minutes before the injection of tribromethanol. The tribromethanol was given in a freshly prepared 3 per cent aqueous solution, which was tested with congo red indicator to insure freedom from the acid products of hydrolysis. The dosage ranged from 0.3 to 0.5 Gm. per kilogram

of body weight. Surgical anesthesia developed within five minutes from the time of rectal administration and lasted for from fifteen minutes to one and one-half hours. It was noted that the more emaciated animals showed anesthesia of greater duration. Respiration was usually slowed, but the pulse rate was not markedly altered. When no preanesthetic dose of morphine was given, doses of from 0.26 to 0.33 Gm. of tribromethanol per kilogram of body weight produced a deep sleep, but the duration of surgical anesthesia was never more than six minutes. The rectal temperature of the animals fell consistently during the anesthesia.

Three animals were given repeated rectal injections of from 0.3 to 0.4 Gm. of tribromethanol per kilogram of body weight, preceded by the usual dose of from 30 to 45 mg. of morphine sulphate. The anesthetic was given at intervals of from two to five days until each animal had received the anesthetic eight, fourteen and twenty times. Two of the three animals had pulmonary infection during the experiment, possibly brought on by unavoidable chilling during the anesthesias. One of the animals had pulmonary and renal tuberculosis. These tuberculous lesions have not been included in the pathologic description. No marked alteration in susceptibility to the anesthetic was noted. All animals, however, lost weight during the series of anesthesias. The animals were finally killed and examined post mortem. The observations at autopsy were as follows:[51]

The heart showed no gross changes. In histologic examination, it showed slight hydropic degeneration.

In one of the three animals, gross inspection of the lungs indicated pneumonia. Histologic examination showed acute bronchial pneumonia in this case and tuberculosis in another case. The lungs of one animal that had received twenty anesthesias were normal both grossly and microscopically.

On gross observation the liver presented possible fat. On histologic examination, the parenchyma showed marked swelling of the cells, which almost obliterated the capillary field. The individual cells were extremely pale and vacuolated, and showed coagulated, eosin-staining granules throughout. The vacuoles were evidently serous rather than fatty. In one case, most of the cells were distinctly atrophic.

Microscopic examination of the kidneys showed congestion of the glomeruli and parenchymatous degeneration of the tubules, with much albumin in the lumen. In two cases, there was some boundary zone necrosis with serous vacuoles in the living cells. In one case, there were localized areas of lymphatic polymorphonuclear infiltration of the interstitial tissue.

There was evidence of damage to the corpuscles of the spleen in all three cases, one showing necrosis, the other two hyperplasia. There was accumulation of hemosiderin in two cases.

The pancreas was normal.

In one case, acute ulcerative colitis was noted.

51. Prof. C. H. Bunting of the Department of Pathology of the University of Wisconsin made the pathologic studies.

Intravenous injection of 3 per cent solution of tribromethanol in physiologic solution of sodium chloride into dogs produced a sudden but brief anesthesia. Doses of from 0.06 to 0.12 Gm. per kilogram of body weight produced surgical anesthesia of from seven to ten minutes' duration. Recovery was rapid.

A 3 per cent solution of tribromethanol in physiologic solution of sodium chloride was administered to several dogs without previous medication. From 2 to 4 cc. per kilogram resulted in instantaneous anesthesia of durations varying with the dosage. Anesthesia was immediate and profound. Recovery was gradual compared with the induction, but rapid compared with the recovery following the use of any other method. For example, a dog weighing 9 Kg. receiving no premedication was given 35 cc. of 3 per cent solution of tribromethanol in physiologic solution of sodium chloride intravenously. Anesthesia was immediate and profound, with complete relaxation, lasting ten minutes. Gradual recovery took place, and eighteen minutes after injection the dog was on his feet and eating a dog biscuit with evident relish.

With the assistance of Prof. E. G. Hastings, of the department of agricultural bacteriology, the effect of tribromethanol on microorganisms was studied. In 3 per cent solution, the drug was found to have a definite bactericidal action.

CLINICAL INVESTIGATION OF TRIBROMETHANOL

In June, 1928, through Dr. Helmut Schmidt we were fortunate in having a clinical demonstration of tribromethanol and the technic of its administration. Following this demonstration, we began a laboratory and clinical investigation of the drug.

In view of the foregoing reports quoted from the literature and the data from the laboratories of pharmacology and experimental surgery of the University of Wisconsin Medical School, we felt that the exceptionally comfortable induction of surgical anesthesia by means of tribromethanol gave promise of filling a real need. Unreasonable and terror-stricken patients, particularly children, are difficult subjects for anesthesia and operation. The rectal administration of ether requires such a thorough preparation and necessitates such elaborate technic that a substitute seemed highly desirable.

The technic which we shall describe and which we have followed largely throughout our work with tribromethanol is based on the instructions originally given us by Schmidt, and elaborated somewhat as a result of our own personal experiences.

TECHNIC

Ward Preparation of Patient.—Sufficient bland enemas (water or physiologic solution of sodium chloride) to empty the lower bowel completely are given as a

routine. As a preanesthetic narcotic, we customarily use morphine and scopolamine, administered by hypodermic injection one and one-half hours before the expected time of administration of tribromethanol. Doses are ordered that we should expect to be satisfactory were an anesthesia from gas-oxygen contemplated. Premedication we believe to be desirable for a satisfactory anesthesia; furthermore, a careful observation of the effect of such premedication is a valuable guide as to the probable need for an increase or reduction of the calculated dose of tribromethanol. Infants are given no premedication.

Preparation of Solution.—The hospital pharmacist delivers crystals to us weighed up in 3 Gm. packets folded in paper, similar to the powders that he prepares for bedside administration of various drugs. These 3 Gm. powders combined with 100 cc. of distilled water, or any multiple of these quantities, are brought into solution by agitation in a 500 cc. Erlenmeyer flask held in a water bath kept at a temperature between 40 and 44 C., or from 104 to 110 F. When complete solution is accomplished, a 5 cc. sample is tested by the addition of from one to three drops of a 1:1,000 congo red solution. If the red changes to purple or blue, the solution is discarded. Fresh solutions are prepared daily.

Dosage.—A basic dose of 0.1 Gm. of tribromethanol per kilogram or 1.5 cc. of a 3 per cent solution per pound of the patient's body weight is usually used.

Instillation.—A 3 per cent solution properly prepared is apparently less unpleasant than distilled water in contact with the rectal mucosa. This is probably due to the mild local anesthetic effect exerted by the drug.

A soft rubber urethral catheter (no. 10 French) is inserted into the rectum past the sphincter muscle. Two strips of adhesive plaster are used to pull the buttocks firmly together around the catheter. Adhesive strips are allowed to cross in the center and have contact with the catheter, thus holding it in place. Care in fixing the catheter firmly in place saves much embarrassment in the prevention of the solutions leaking out after muscular relaxation has developed. A 50 cc. glass syringe is found convenient with which to measure and inject the solution, which should be at body temperature. Extremely slow injection of the first 50 cc. is preferable, because apparently the local anesthetic effect on the rectal mucosa obtunds the rectal reflex with tendency to expulsion of the solution.

Supplemental Anesthesia.—It seems to us highly desirable that the final accomplishment of complete surgical anesthesia be dependent on a drug under quick control. The variations in tolerance of drugs by different persons is so great that an attempt to predetermine what dose will accomplish surgical anesthesia in a given person is dangerous. We attempt, therefore, by means of tribromethanol, to deepen the sleep of a patient to a plane from which surgical anesthesia can be easily reached with a light dosage of nitrous oxide. Whatever the inhalation agent used to complete anesthesia begun by tribromethanol, the dosage must be carefully regulated, and an abundance of oxygen and a free airway assured.

It seems justifiable in some cases to prolong the effect of tribromethanol during an extremely long operation by further instillations of the drug during operation. For the ordinary operation, lasting less than ninety minutes, additional quantities of tribromethanol may result in a deep anesthesia at the end of operation, accompanied by abolished reflexes, at a time when the patient must pass from the careful supervision of the anesthetist to that of the busy ward nurses. In most instances, therefore, supplementation with nitrous oxide is recommended in preference to additional instillations of tribromethanol.

Supervision.—In no case does the anesthetist fail to follow his patient through the operation with the minute supervision which he would accord patients anesthetized by inhalation of anesthetic gases or vapors. Pharyngeal airways are used

in most cases, and oxygen is added through them on many occasions. This practice is followed because we feel that oxygen is a factor of no small moment in the successful administration of other agents, and that a new drug deserves like consideration. In addition, it appears to us that many of the untoward results reported by others could be ascribed to effects secondary to respiratory obstruction and anoxemia. The excellent relaxation of pharyngeal muscles accompanying this form of anesthesia justifies such a conclusion.

Careful supervision during the period of anesthesia is just as necessary with this drug as with any drug administered by inhalation. Our one unfortunate experience occurred in a case in which complete deep anesthesia was attempted with tribromethanol alone. A child, 18 months old, weighing 24 pounds (10.9 Kg.), whose calculated dose was 36 cc. of a 3 per cent solution, was given a dose of 50 cc. Operation was begun ten minutes after instillation. The child was of the type subject to respiratory obstruction on the slightest provocation. The period of operation was characterized by difficulty in maintaining a clear airway, and anesthesia was still present when the operation was finished. The child was allowed to go back to the ward, without an artificial pharyngeal airway. Respiratory obstruction supervened three hours later, in the absence of sufficient supervision, and death resulted. The same accident would doubtless have occurred had the child been given ether in extreme dosage, and had the same faulty supervision existed. In no case should the patient be left without supervision before pharyngeal reflex and muscular tone have returned. Metal pharyngeal airways in place during operation and thereafter until no longer tolerated seem essential in tribromethanol anesthesia. The advantage of controlling the final depth of anesthesia with a labile agent, such as nitrous oxide, which can be adjusted at one's finger-tips, is evident. Under no circumstances should the supply of oxygen be deficient. An excess of oxygen and correction of a faulty airway often "smooth out" an anesthesia that appears to be insufficiently deep.

OBSERVATIONS

Tribromethanol has been used at the Wisconsin General Hospital in 234 clinical cases. Selection of these cases was made to cover as wide a range of risks as possible, as well as to cover a wide variety of surgical procedures. An analysis of the first 100 cases follows:

Induction.—The absorption of the drug by the circulation following rectal instillation appeared to us to result in a normal "going to sleep." Children without previous opiates sometimes yawned and announced that they felt sleepy during the induction, but seldom complained of discomfort. Children who had already undergone the ordeal of the ward enema were happily relieved to find that this was so much easier. Unconsciousness usually came on within from three to five minutes from the beginning of instillation. Just as one child was going to sleep, she whispered the statement that she felt sick at her stomach. This was the nearest to evidence of nausea that we encountered during induction. In the total number of cases, we did not see vomiting occur during either induction or operation, in spite of the fact that in most of the cases anesthesia was administered for operations on the head, and in many it appeared to be light.

The pharyngeal reflex was abolished early, so that a rigid pharyngeal airway could usually be inserted long before operation was begun. Our impression is that the laryngeal reflex disappears only with excessive dosage. If this impression is borne out by more extensive experience, it is of the greatest value in anesthesia, since the activity of the "watch-dog of the lungs" is highly desirable during the period of unconsciousness. There was no tendency to an excessive secretion of mucus in the mouth and pharynx, even in the patients not receiving premedication. The skin reflex, or muscular reaction as the result of incision of the skin, disappeared late. This proved an embarrassment in cases of circumcision and perineorrhaphy.

Muscular relaxation suitable for laparotomy was often secured with the calculated dose mentioned. Our impression is that with increasing dosage of tribromethanol ascending paralysis of the spinal cord takes place, similar to that seen with increasing dosage of ether. We noted at least two cases in which there was partial intercostal paralysis. In both of these cases, the systolic blood pressure dropped during the respiratory depression. We see no advantage in an increase of the dosage of tribromethanol to accomplish complete anesthesia. We prefer to add a more labile agent that can be introduced and exhaled through the alveolar walls.

Duration of Anesthesia; Recovery.—With the use of a solution of tribromethanol, prepared from crystals of tribromethanol, recoveries compared in length of time with those from anesthesia from ether.

After-Effects.—No clinical evidence of proctitis or other irritation was noted in any case. Restlessness after the use of the solution prepared from crystals was not frequent or marked.

Urinary Changes.—An attempted analysis of preoperative and postoperative urinary observations, as reported through routine laboratory analyses by hospital technicians, shows changes comparable to those found after operation in which other anesthetic agents have been employed. We do not believe these determinations to be of consistent value, but present them as we found them.

No case of suppression of urine was noted. Analysis of sixty-four urinary records gave the following figures: In twelve cases, the postoperative specimen of urine gave a positive result in the test for acetone, acetone not being noted in the preoperative specimen; in ten cases, casts were shown; in twelve, albumin. On the other hand, in nine cases the test for albumin gave negative results after operation, whereas there had been positive results before operation. No clinical evidence of damage to liver or kidneys came to our notice. The care with which respiratory obstruction and anoxemia were avoided may account for the absence of damage to liver or kidneys.

Alterations of the Blood Chemistry.—Study was made in a few cases (fifteen) of some of the chemical constituents of the blood before and after anesthesia produced with tribromethanol, to ascertain whether any changes would be revealed as an immediate effect of the drug. For this purpose, blood was taken from the patient's vein just previous to rectal instillation, and again immediately following the completion of operation. The average length of time elapsing between the taking of the two samples was from an hour to an hour and a half. Determinations of nonprotein nitrogen, sugar, alkali reserve (carbon dioxide-combining power of plasma) and sodium chloride were made on each sample. From the results presented in table 3, it will be seen that no significant or consistent changes were noted. No information is at hand for judging the possibility of delayed changes.

TABLE 3.—*Blood Chemistry in Anesthesia from Tribromethanol*

	Preanesthetic				Postanesthetic			
Case	Sugar, Mg.	Nonprotein Nitrogen, Mg.	Sodium Chloride, Mg.	Alkali Reserve, Mg.	Sugar, Mg.	Nonprotein Nitrogen, Mg.	Sodium Chloride, Mg.	Alkali Reserve, Mg.
1.....	96.0	33.9	479	29.4	111	34.7	462	43.7
2.....	103.0	40.7	432	36.5 (hemolyzed)	119	38.2	430	33.6 (slightly hemolyzed)
3.....	80.0	34.4	465	51.4 (hemolyzed)	110	29.0	447	....
4.....	86.0	40.5	340	Sample short	105	37.4	316	36.0
5.....	80.5	22.6	449	52.1	144	22.3	465	35.4
6.....	61.5	33.6	432	27.2 (badly) hemolyzed)	116	35.8	469	23.9
7.....	84.0	38.9	485	41.7 (slightly hemolyzed)	122	34.0	452	29.9

The rise in blood sugar is decidedly less than similar observation has revealed with various inhalation agents. Other changes are within the range of experimental error. The changes noted are in essential agreement with those reported by Wymer and Fuss.[23]

Somatic vs. Psychic Effect.—The following case is described in detail because it illustrates the fact that apparently tribromethanol is primarily a somatic sedative and not a cerebral sedative. A knowledge of this fact is essential to a proper use of the drug.

A young man was seen suffering from acute manic-depressive psychosis, manic phase, of three weeks' duration. He could not be quieted by excessive doses of morphine paraldehyde, chloral, etc. When given 0.1 Gm. of tribromethanol per kilogram by rectum, he became somewhat relaxed, but responded to the slightest stimulation of the cerebrum, and if spoken to, would sit up in bed and talk wildly. The slight effect of the drug passed off in less than two hours. Three days later, this patient was given 0.2 Gm. of sodium *iso*-amylethylbarbiturate

intravenously, after which he slept soundly. The injection was continued to a total of 0.5 Gm. of sodium *iso*-amylethylbarbiturate, with the result that the patient slept for seven hours, awoke, ate dinner and again slept or was quiet for eight hours.

Many other cases could be cited to show that tribromethanol is in effect primarily a somatic sedative, becoming a psychic sedative only in large doses. For this reason, we feel that scopolamine is a highly desirable adjuvant in combination with tribromethanol.

In view of the possibility of damage to the liver and kidneys from the use of tribromethanol, 2 cases of cholecystectomy in which a rather high degree of damage to the liver was present, and 5 of nephrectomy in which the other kidney was in none too good condition, were included in the aforementioned 100 cases. In each of these cases the patient made a satisfactory recovery. In each, oxygen was freely displayed through the pharyngeal airway throughout the operation.

Amylene Hydrate Preparation.—A preparation at one time forwarded by the manufacturers, namely, a solution of tribromethanol in amylene hydrate, carried 1 Gm. of tribromethanol per cubic centimeter. We used this preparation in place of the crystals for one month, with the following observations:

1. Amylene hydrate lends a distinctly unpleasant odor to the solution, and this odor is exhaled by the patient during anesthesia.

2. The mixing of this solution with distilled water we found to be nearly as difficult as was solution of the crystals of tribromethanol in distilled water. Small globules of amylene hydrate solution tended to remain separate and were less easily noted than was incomplete solution of crystals.

3. Measurement of a liquid by means of a pipet or graduated cylinder seemed less accurate in our hands than the handling of powders weighed out by the hospital pharmacist.

4. It seemed to us that a larger proportion of persons anesthetized with a 3 per cent solution of tribromethanol made by means of the amylene hydrate preparation showed irrationality and uncontrollable restlessness during recovery than of persons anesthetized by means of the crystal preparations and that the period of postanesthetic sleep for the former was longer. Unless there is a distinct advantage in convenience of manufacture and marketing in favor of the amylene hydrate preparation, we see no advantage in the introduction of a mixture of two active drugs when one will serve as well. A preoperative and postoperative proctoscopic study of the crystal and fluid preparations of tribromethanol is in progress.

Intravenous Use of Tribromethanol.—Kirschner [52] recently suggested the intravenous use of this drug. A 3 per cent solution is made in physiologic solution of sodium chloride, and 1 cc. for each kilogram of the patient's body weight is injected into a vein during an interval of forty-five seconds. Kirschner stated that anesthesia follows instantly and is complete, and that recovery occurs within fifteen minutes.

The startlingly rapid induction and recovery that we had previously noted in dogs when tribromethanol was given intravenously, together with the lack of symptoms following, led us to administer tribromethanol intravenously to seven patients in whom a temporary profound anesthesia was needed. Two were given 1 cc. of 3 per cent solution of tribromethanol in physiologic solution of sodium chloride per kilogram of body weight. The injection was as rapid as possible. No premedication was used. In each patient, immediate anesthesia resulted, in one deep and in the other light. Both awakened ten minutes later. One ate his lunch on returning to the ward one-half hour after injection.

One patient was given a similar dose (1 cc. per kilogram) without premedication, the injection being given slowly, and a light anesthesia was maintained for twenty minutes. A fourth case demanded deep anesthesia for fifteen minutes. The patient had just received one-sixth grain of morphine sulphate hypodermically. He was given 90 cc. of 3 per cent solution instead of 63 cc., which was the calculated dose at 1 cc. per kilogram. Profound anesthesia, with slow pulse and depressed respiration, lasted five minutes followed by deep anesthesia, with normal pulse and slow deep respirations gradually lightening to phonation and muscular movements twenty minutes after injection. He was awake twenty-three and one-half minutes after injection and asked for cigarets. During the next four hours he complained of pain in the upper part of the abdomen whenever awake, but he slept a great deal during that time. He then ate dinner and vomited afterward. He also vomited his breakfast the next morning, and still complained of pain in the upper part of the abdomen. Later that day he was discharged from the hospital, feeling fit. No other case of abdominal pain or nausea occurred when anesthesia was produced by tribromethanol given intravenously. One patient, in whom two attempts had been made to obtain anesthesia with intravenous injection of tribromethanol, was found at the third attempt to have a thrombosis of each median basilic vein, extending several inches above the point of injection. No other instances of thrombosis have been noted.

Further study as to the safety of intravenous administration of tribromethanol is indicated. A method of producing complete, profound

52. Kirschner, M.: Eine psycheschonende und steuerbare Form der Allgemeinbetäubung, Chirurg. **1**:673, 1929.

and extremely short anesthesia has possibilities of usefulness in carefully selected cases. The extremely rapid detoxication of tribromethanol, when it is administered intravenously, is interesting.

SUMMARY AND CONCLUSIONS

A review of the literature concerning tribromethanol is presented. Certain laboratory data are recorded verifying and extending the experimental work of previous investigators. The points of major interest are:

1. When kept at ordinary room temperatures, 3 per cent solutions of tribromethanol are stable toward hydrolysis for a period of approximately from twenty-four to forty-eight hours following their preparation.

2. Anesthesia obtained with tribromethanol in animals indicates that the drug has approximately the same margin of safety as other drugs commonly used in the production of general anesthesia. The anesthetic dose is approximately from two thirds to three fourths of the fatal dose.

TABLE 4.—*Statistics on One Hundred Cases in Which Anesthesia Was Obtained with Tribromethanol*

Average:	
Age (range from 4 days to 74 years)	24 years
Weight	88 pounds (39.9 Kg.)
Calculated dose (3 per cent aqueous solution)	132.8 cc.
Given dose	150 cc.
Length of operative procedure	53 minutes
Length of supplemental anesthesia	25 minutes
Length of induction period	20 minutes
Duration of sleep	3½ hours
Patient morphinized	83 per cent
Patient nonmorphinized	17 per cent
Tribromethanol supplemented	71 per cent
With gas (nitrous oxid and oxygen)	50 per cent
With procaine or cocaine hydrochloride	21 per cent
Tribromethanol unsupplemented	29 per cent
Respiratory and Circulatory Changes:	
Pulse—Rise or fall more than 20 per minute from normal	13 per cent
Systolic—Rise or fall more than 20 mm. Hg from normal	11 per cent
Respiration—Under 20 per minute	2 per cent
Between 20 and 30 per minute	70 per cent
Over 30 per minute	28 per cent
Shock	2 per cent*
Recovery:	
Nausea or vomiting (72 hours)	22 per cent†
Marked restlessness	12 per cent
Distention	5 per cent‡
Marked perspiration	4 per cent
Headache (nasal)	3 per cent
Deaths	2 per cent§

* One, a patient operated on for tumor of the brain; the other, a woman brought to the operating room with streptococcus septicemia secondary to neglected infection of the abdominal wall.

† Seventeen per cent of these were cases in which the patient swallowed blood in the course of an operation on the mouth or the face.

‡ All were cases in which laparotomies or nephrectomies were done, the distention occurring on the third day following operation.

§ A patient with tumor of the brain who died ten and a half hours following operation, and one with a cleft palate, who died three hours following operation.

3. Animals in which anesthesia has been obtained repeatedly show no noticeable variations in susceptibility to the narcotic action of the drug. Following repeated anesthesia, dogs show pathologic changes in the kidneys, liver and spleen. The type of lesion is not that characteristic of the intoxication caused by chloroform.

4. Tribromethanol acts as a prophylactic against the convulsive effect of toxic doses of procaine hydrochloride and cocaine in rabbits. Under tribromethanol anesthesia the fatal dose of these local anesthetics is increased from 50 to 200 per cent, respectively.

Record is made of our experiences with the clinical administration of this drug in 100 cases. The patients represented a wide range of surgical risks, in order to afford a fair test of the usefulness and safety of the drug. Analysis of these experiences leads us to the following conclusions:

1. As does the use of other anesthetic agents administered orally, intravenously, subcutaneously and rectally, the use of tribromethanol necessitates a predetermined dosage, which involves an element of chance as to the proper amount to be given to each individual.

2. If proper precautions are observed in the preparation of solutions, we feel that we can safely administer the drug in doses not exceeding 0.1 Gm. per kilogram of the individual's body weight, in most cases.

3. Since tribromethanol is a somatic rather than a psychic depressant, we feel that proper psychic depression with such drugs as scopolamine administered hypodermically or derivatives of barbituric acid administered orally should precede its use in cases in which anxiety is a factor. Moderate doses of opium derivatives can wisely be used as adjuvants. This combination of hypodermic, oral and rectal administration should preferably accomplish an effect short of complete surgical anesthesia.

4. Nitrous oxide with an excess of oxygen has been found satisfactory in the accomplishment of final anesthetic control.

5. An artificial pharyngeal airway for the maintenance of free breathing through the relaxed pharynx is essential in every case. Oxygen flowing through the airway is of distinct benefit to the patient.

6. The absence of gastro-intestinal irritation, together with the freedom with which oxygen can be administered, accompanying this agent, appears to make its use justifiable in cases of severe damage to the kidneys and liver, provided minimum dosage is employed.

7. No advantage appears to result from the use of tribromethanol "fluid" (67 per cent tribromethanol + 33 per cent amylene hydrate) in place of crystalline tribromethanol for the preparation of anesthetic solutions. In our hands, the crystalline form of the drug gave more

satisfactory results than the amylene hydrate solution. As noted before, a comparative proctoscopic study of the possible rectal irritation from the crystal and fluid forms of the drug is in progress.

8. Alterations in blood chemistry under anesthesia from tribromethanol, as herein described, are probably not clinically significant.

9. The only antidote for overdosage so far found useful is maintenance of a free airway and administration of oxygen, with the addition of small amounts of carbon dioxide when indicated. In extreme overdosage, artificial respiration with oxygen should be utilized.

10. The possible usefulness of tribromethanol administered intravenously in extremely short operations deserves trial and investigation in view of the pleasant and quick induction and recovery without gastro-intestinal disturbance.

11. The need for experience and careful attention on the part of the anesthetist as to dosage and supervision is in no way less than with the agents now in common use.

12. Justification for the addition of tribromethanol to the present well recognized list of anesthetic drugs probably rests chiefly on the fact that it brings one a step nearer perfect induction of anesthesia. Induction by means of a simple, nonpainful rectal instillation, without preparation with other drugs, fills a need in the present armamentarium.

BLUE-DOMED CYSTS AND CANCER OF THE BREAST *

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The etiology of cysts of the breast furnishes a field for interesting speculation, and many theories have been advanced to explain their origin and development.[1] Cheatle's [2] study of sections of the entire breast shows the relation of cysts to the epithelium of the ducts and acini.

Two varieties of cysts may be separated according to the character of the cyst wall. In the first, the wall is lined by one or more layers of epithelial cells, and either is smooth or shows papillary ingrowths. In the second, the epithelial lining is absent or fragmentary and degenerative.

In the first variety the cysts are small, mutliple tumors which contain clear, cloudy, milky or bloody fluid. The epithelial lining of these cysts is derived more often from the duct than from the acinus, and the cysts are due not to mechanical obstruction from the outside, but to epithelial proliferation in the duct. In the second variety the cysts are large; clinically, they usually are single tumors; when exposed by an incision, they appear as blue, smooth, rounded masses, an appearance which gives them the name, blue-domed cyst.

With obstruction, secretion from the epithelium fills the lumen of the duct and acinus with fluid of varying quality. Accumulation of the fluid distends the obstructed area and produces a mass more or less spherical in outline. If the distention is sufficient, pressure within the spherical cyst interferes with the nutrition of the epithelium, so that this portion of the wall becomes fragmentary or disappears. During this time, chemical changes taking place in the accumulated fluid alter its character. When the epithelium of the cysts is of direct origin, the breast about the cysts will contain many dilated ducts, but dilatation of the acini is not necessarily present.

The papillomatous cyst contains bloody fluid or grumous material. Cheatel declared that he had never seen a breast that contained only a single cyst. With the papillomatous cysts this is an important fact, because these tumors undoubtedly have malignant potentialities.

There is no evidence that the smooth-walled epithelial-lined cyst is prone to malignancy, and there is no evidence that the danger is proportional to the size of the cyst, but it has been found that any sized cyst may contain papilloma and primary carcinoma.

* Submitted for publication, March 25, 1930.

1. Goldzieher, M. A., and Kaldor, J.: Cystic Cirrhosis of the Breast, Arch. Surg. **20**:473 (March) 1930. Rodman, J. Stewart: Chronic Cystic Mastitis: Preliminary Report of the Nature of the Process, Arch. Surg. **20**:515 (March) 1930.

2. Cheatle: Brit. J. Surg. **8**:149 (Oct.) 1920; ibid. **9**:235 (Oct.) 1921.

The blue-domed cyst from the wall of which the epithelial lining has disappeared cannot become the seat of cancer. Because this tumor is benign and so seldom associated with carcinoma, extremely conservative methods of treatment have been recommended. Many years ago Abbey advised aspiration of the cysts, but the method was soon abandoned, because it gave no opportunity for examination of the wall of the cyst or the surrounding breast tissue. Recently, Bloodgood [3] advised that when a patient whose original tumor is a blue-domed cyst, comes back with a similar lump in the same or the opposite breast, it is his rule not to reoperate.

The clinical signs of blue-domed cyst are fairly distinct, and usually the diagnosis can be made with a reasonable degree of accuracy. The tumor is spherical, often fluctuates, and is not fixed in the tissues. The surrounding breast is lumpy rather than shotty and it is rare to find dilated ducts beneath the nipple. Transillumination of the breast shows a clear area in the position of the tumor. Often the tumor is painful or tender, and there is a history of variation in its size at different times. Sometimes there is a clear history of the spontaneous disappearance of a similar tumor followed by the development of the one under investigation.

In spite of these distinct characteristics, no clinical examination can show the condition of the cyst wall. In certain rare instances the wall contains an area of active epithelium, which is potentially malignant. Adams [4] reported a case in which cancer developed in such an area in a blue-domed cyst. Bloodgood admitted that cancer was present in 1 per cent of his 500 cases, but pointed out that in these cases the malignant tumor was diagnosed before operation. In a series of 100 cases of cancer of the breast, I have had 3 in which carcinoma and blue-domed cyst were present at the same time; in these cases the cancer was recognized by clinical signs, but there must have been a period in the course of the disease when it was not so evident. Therefore it is better to excise all blue-domed cysts and to study the surrounding breast tissue as well as the wall of the cyst for areas of malignancy.

The large cyst practically never is a single tumor, and all the small cysts contain actively proliferating epithelium, with or without papillomatous ingrowths. Our experience with papillomatous cysts has not been as encouraging as Dr. Bloodgood's.[5] In a series of 100 cases of cancer of the breast, 5 showed cancer developing in a papillomatous cyst.

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3. Bloodgood, J. C.: Blue-Domed Cyst in Chronic Cystic Mastitis: Its Relation to Cure of Cancer, to Benign Lesions of the Breast and to Educational Program, J. A. M. A. **93**:1056 (Oct. 5) 1929; The Blue-Doomed Cyst of Chronic Cystic Mastitis in the Breasts of Women, ibid. **93**:1163 (Oct. 12) 1929.

4. Adams: Canad. M. A. J. **19**:190 (Aug.) 1928.

5. Bloodgood: Am. J. M. Sc. **179**:32 (Jan.) 1930.

In 8 benign papillomatous cysts all the specimens showed the presence of multiple growths. One specimen was the second breast removed from a patient who had been operated on for carcinoma in the other breast. The cancer in the first breast was an infiltrating scirrhus in the nipple zone.

One woman who had a bloody discharge from the nipple was examined at monthly intervals for more than a year, and no palpable tumor could be found. She returned six months later with a tumor in the nipple zone, which was clinically malignant. She was operated on by another surgeon, who reported that the tumor was a carcinoma in a papillomatous cyst. In dealing with cysts of the breast too great conservatism is dangerous. In my opinion, the blue-domed cyst as well as the papillomatous cyst should be excised in all instances, and the cyst wall carefully studied.

With recurrent blue-domed cysts, repeated excisions may become necessary, and in instances of recurrence, therefore, removal of the breast should be advised. These patients usually are at the menopause; the breasts are small, and the removal of one or both is a slight disfigurement. The 1 to 3 per cent possibility of concurrent malignancy is thus avoided.[6]

The following is a summary of the records in three instances of the simultaneous presence of cancer and blue-domed cyst of the breast.

REPORT OF CASES

Case 1.—A white woman, aged 48, was admitted to the hospital on Sept. 22, 1925. She was married but had never been pregnant. The duration of the tumor was six months. There were two smooth, rounded masses just below and to the outer side of the nipple, extending into the upper inner quadrant of the left breast. To the inner side of these masses there was a hard, sharp-edged tumor, about 1 inch (2.5 cm.) in diameter, over which the skin dimpled when the breast was lifted forward from the chest wall. The right breast was free from lumps. General clinical examination was negative for evidence of other lesions.

The complete operation for cancer was performed on September 24. The note made at the time of operation mentioned that fibrosed lymphatic glands were found in the axilla, but that the vein was not adherent. The wound was closed with a skin defect on the chest wall, which was covered with pinch grafts six days later. The patient made a good recovery and was discharged on the twentieth day following operation.

The tumor was a scirrhous carcinoma about 1½ inches (3.8 cm.) in diameter, with infiltrating projections for a considerable distance in all directions. On the inner side of the cancer between it and the skin about the nipple, there were two large blue cysts, each about 1½ inches in diameter. Both cysts were fixed to the carcinoma, but apparently the fixation came from infiltration of the cyst wall by

6. Fischer, W.: Clinical and Pathologic Anatomic Diagnosis of Tumors and Cystic Transformation in the Mammary Gland, Deutsche Ztschr. f. Chir. **192**:1, 1925.

the carcinoma rather than from extension of a primary tumor from the cyst wall.

On Jan. 25, 1926, a little more than three months later, she returned with a mass in the right axillary prolongation of the right breast. She had noticed the tumor while bathing the day before. The tumor was clinically malignant, hard, sharp-edged and fixing the skin. The complete operation was performed on the right side on January 27. The axilla appeared favorable; the wound was closed with a skin defect, which was grafted four days later. The patient again made a good postoperative recovery and was discharged on Feb. 16, 1926.

The tumor from the right breast was a small, infiltrating scirrhous. Just beyond the tumor toward the axilla there was blue-domed cyst about 1 inch in diameter, and around the solid cancer there were a number of small blue cysts. At no place could a connection between the cancer and the walls of a cyst be found.

The patient remained well for about a year, and then began to show signs of metastasis of the spinal roots. She died with evidence of general carcinosis two years after the first operation.

CASE 2.—A colored woman, aged 38, was admitted on Oct. 19, 1928, complaining of lumps in the right axilla. There were three separate masses, the lowermost one being on the border of the pectoralis major at the base of the axilla and the others higher up in the space. The masses were smooth and a little tender, and the lowermost one was attached to the skin for a short distance. There were no lumps or tender areas in the breast and no wounds or scars of the hand or arm.

General clinical examination gave negative results, and laboratory tests threw no light on the probable nature of the masses.

At operation the upper smooth masses were found to be blue-domed cysts, and the lower one a papillomatous cyst, containing blood and showing an indurated and infiltrating wall. The complete operation for cancer was performed. The fat along the axillary vein was soft, and no fibrosed lymphatic glands were noted. The wound was closed without grafting. The patient made a good recovery, and when seen one and one half years later was well.

No tumors were found in the normally situated breast tissue. The blue cysts and the malignant papillomatous cyst were situated in an axillary mass of breast tissue, which appeared to be a separate development rather than an extension of the axillary prolongation of the breast. The wall of the blue-domed cyst was distinct from that of the papillomatous cyst, and there was no infiltration between them.

Supernumerary breasts and aberrant masses of breast tissue are well known congenital anomalies. The unusual breast tissue often does not attract attention until it hypertrophies during lactation or becomes involved in tumor formation.

The axilla is a frequent seat of accessory breasts. As a rule, the supplementary tissue can be identified without question. McFarland [7] pointed to the close resemblance between the large sweat glands of the axilla and mammary tissue as a possible source of error in determining the nature of an axillary tumor. In the present case the blue cysts as well as the papillomatous one seemed to be definite indications that the tumor originated in breast tissue.

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7. McFarland: Am. J. Path. **5**:23 (Jan.) 1929.

SKELETAL METASTASES FROM CARCINOMA OF THE RECTUM

REPORT OF EIGHT CASES *

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Since the advent of the widespread use of the roentgen ray for diagnosis, there has been a great increase in the knowledge of those neoplasms that cause osseous metastases. Carcinomas of the prostate, breast, thyroid and pulmonary bronchus, as well as hypernephromas, have been known to be the most common producers of secondary growths in the skeletal system. Primary carcinomas of other organs do cause metastases in the bones, and these occur with sufficient frequency to make their clinical recognition an important factor in the amelioration of their symptoms.

Skeletal metastases occur in 10.5 per cent of rectal carcinomas according to Nisnjewitsch,[1] who found them in six of fifty-seven postmortem examinations. The determination of the true percentage of such occurrences is impossible from either a clinical or a pathologic standpoint unless the material is examined carefully with that point in view. Miyauchi [2] examined the lumbar vertebrae in thirty-five consecutive postmortem examinations of patients with cancer and found five with gross metastases; in another five, metastases were found only on microscopic examination.

Skeletal metastases were found in 8 cases of rectal carcinoma at Montefiore Hospital during the period from Jan. 1, 1922, to March 1, 1930. During this time 117 patients were admitted with the diagnosis of carcinoma of the rectum. Of these, 78 died in the hospital and there were 29 autopsies. A careful search of the literature revealed only 16 reported cases of bone metastases in carcinoma of the rectum.

The first case of rectal carcinoma with bone metastases was reported by Curling [3] in 1870. This occurred in a man 48 years of age, who had

* Submitted for publication, April 14, 1930.

* From the Surgical Service, Montefiore Hospital. Dr. Harold Neuhof, Chief of Division.

1. Nisnjewitsch, Leo.: Die Metastasen des Karzinoms in das Knochensystem, Inaugural Dissertation, Basel, 1907.

2. Miyauchi, K.: Zur Kenntnis der Karzinommetastasen im Knockensystem, Inaugural Dissertation, Basel, 1916.

3. Curling, T. B.: Case of Cancerous Stricture of the Rectum Producing Obstruction, Successfully Relieved by Colostomy, Lancet **1**:3, 1870.

had a colostomy performed for rectal obstruction seventeen months before death. The postmortem examination showed a cancer of the rectum invading the posterior wall of the pelvis and sacral plexus. "A large tumour had formed at the right elbow which seemed to be a deposit of soft cancer in the upper part of the radius distending the bone."

Hildebrand,[4] in discussing statistics of rectal carcinoma, reported the case of a man, aged 59, with a history of having had the condition for eighteen months, in whom metastasis developed in the upper end of the femur seven months following proctectomy. Hochenegg [5] reported a case in which a Kraske resection had been performed and in which the patient nine months later had a spontaneous fracture of the right scapula due to metastasis. In addition to this fracture, the presence of metastases to the lungs, liver, peritoneum, kidney and suprarenal glands, was confirmed post mortem. Both of these cases were reported in 1888.

In 1891, Pitts [6] reported a case of spontaneous fracture of the right humerus eighteen months after colostomy for intestinal obstruction due to rectal carcinoma. Because of pain and nonunion, amputation was done at the shoulder joint, with uneventful recovery. Pathologic examination revealed "a columnar cell carcinoma so perfect in character that it would be impossible to distinguish it from a similar growth in the rectum."

Fuzinami,[7] in 1897, described a case of spontaneous fracture of the femur after the patient had complained of pain in the bone for two months. There had also been diarrhea and an enlarged liver. At postmortem examination, a cylinder cell carcinoma of the rectum was found with metastases to the liver and femur. The growth in the femur was of the same type as that found in the rectum. The author remarked that, according to his experience, such a metastasis was among the greatest of rarities.

In 1906, Goetsch [8] reported a case of metastases to the ribs, vertebrae and femur from a rectal carcinoma. Oehler,[9] in discussing the results of

4. Hildebrand, O.: Zur Statistik der Rectumcarcinoma, Deutsche Ztschr. f. Chir. **27**:329, 1887-1888.

5. Hochenegg, J.: Die sacrale Methode der Exstirpation von Mastdarmkrebsen nach Prof. Kraske, Wien. klin. Wchnschr. **1**:348, 1888.

6. Pitts, B.: Columnar Carcinoma of the Humerus Following Tumour of the Upper Part of the Rectum, Tr. Path. Soc. London **42**:267, 1891.

7. Fuzinami: Casuistische Mitteilung primäre Rectumbrebs mit Spontan Fractur linken Oberschenkelknochen, Arch. f. path. Anat. **147**:129, 1897.

8. Goetsch, W.: Ueber den Einfluss von Karzinommetastasen auf das Knochengewebe, Beitr. z. path Anat. u. z. allg. Path. **39**:218, 1906.

9. Oehler, J.: Ueber Rectumcarcinome, zugleich ein Beitrag zur Lehre von den metastatischen darm Carcinomen, Beitr. z. klin. Chir. **87**:593, 1913.

operative intervention on rectal carcinoma, mentioned one case in which six years after operation, without any local recurrence, metastatic growths in the pelvic lymph nodes and a large secondary tumor of the occipital bone developed.

Mielecki,[10] in reviewing 560 autopsies in cases of cancer found 3 metastases to bone in 56 intestinal carcinomas. One of the cases was a rectal neoplasm. Deelman,[11] in reporting 27 cases of bone metastases from various primary tumors, found 1 from a rectal carcinoma; the site of metastasis was in the vertebrae.

Mandl,[12] in reviewing 779 operations for rectal tumor in Hochenegg's clinic from 1906 to 1920, found 3 cases of bone metastases in 64 postmortem examinations; 1 to the sacrum and spine; 1 to the ribs and 1 to the sternum. He felt that there had been a great increase in the number of bone metastases in later years, and ascribed it to a lessened resistance of the human organism.

Joll[13] described three specimens in the British Museum of osseous metastases from rectal carcinomas. The one specimen is the early case described by Pitts; the second, metastasis to the sternum and spine in a patient 35 years of age, and the third, a metastasis to the ulna.

Jenkinson,[14] in reviewing skeletal growths secondary to malignant intestinal (all parts) conditions, cited among the rectal cases those of Goetsch and Deelman and added one of his own with metastasis to the spine. Jacobs,[15] who reviewed the cases at Montefiore Hospital from 1914 to 1924 in respect to roentgen therapy, mentioned that bone metastasis occurred in four. Siburg,[16] in 1929, reported a case of carcinoid of the rectum with metastases to the lymph nodes and to the thoracic and lumbar vertebrae.

REPORT OF CASES

Case 1.—S. L., a man, aged 44, was admitted to the hospital on Aug. 24, 1921, with a history of blood in stools, difficulty in moving bowels and painful defecation for four years. He had had a rectal operation four years before

10. von Mielecki, W.: Anatomisches und kritisches zu 560 Obductionen bei denen sich bösartige Geschwülste fanden, Ztschr. f. Krebsforsch. **13**:505, 1913.

11. Deelman: Het metastatisch carcinoom in het beenstelsel, Nederl. tijdschr. v. geneesk. **65**:1048, 1921.

12. Mandl, F.: Ueber den Mastdarmkrebs, Deutsche Ztschr. f. Chir. **168**:145, 1922.

13. Joll, C. A.: Metastatic Tumours of Bone, Brit. J. Surg. **11**:38, 1913-1924.

14. Jenkinson, E. L.: Primary Carcinoma of the Gastro-Intestinal Tract Accompanied by Bone Metastases, Am. J. Roentgenol. **11**:411, 1924.

15. Jacobs, A. W.: Carcinoma of Rectum and Sigmoid: Analysis of 121 Cases; Results of Treatment by Radiation, Surg. Gynec. Obst. **43**:50, 1926.

16. Siburg, F.: Ueber einen Fall von sogenannten Karzinoid des Rektums mit ausgedehnter Metastasenbildung, Frankfurt. Ztschr. f. Path. **37**:254, 1929.

admission, which was followed by good health (except rectal incontinence) until February, 1921. Colostomy was performed in May, 1921. For two weeks before admission, he had pain in both legs. Examination showed a fairly well nourished man who had had a left inguinal colostomy. There was a scar from a former rectal operation with resection of part of the sacrum. There was a hard, nodular, polypoid mass protruding from the anus, with hard nodules in the skin. The anal orifice did not permit insertion of finger. There was an enlargement of the left inguinal glands.

Roentgen examination on Sept. 7, 1921, revealed "several small, irregular areas of bone absorption within the right os ischii and a small, irregular area of bone absorption in the infratrochanteric region of the left femur. These areas are characteristic of metastatic growths." A painful area with swelling developed over the upper part of the sternum. On Dec. 28, 1921, the roentgen rays revealed a circumscribed area of bone condensation the size of a half dollar, occupying the middle third of the sternum. The patient slowly became worse, and died on Jan. 9, 1922.

Autopsy revealed a carcinoma of the rectum with an extension into the pelvic tissues and metastases to the regional and distal lymph glands, lungs, calvarium, dura, heart, capsule of the left kidney, ribs, sternum, lumbar vertebrae and sacrum. Bilateral hydro-ureter and hydronephrosis due to ureteral obstruction by tumor tissue was revealed.

CASE 2.—C. B., a man, aged 50, was admitted to the hospital on June 29, 1923, with a history of chronic colitis and rectal polyposis for fourteen years. Colostomy had been done in 1910 for the relief of colitis. The patient had had pain in the right foot, back and spine for three months before admission.

Examination revealed an enlarged liver and enlarged inguinal glands. Examination of the rectum revealed large nodular, infiltrating carcinomatous masses. A biopsy specimen was reported to show adenocarcinoma.

Roentgen-ray examination on July 5 showed small areas of bone destruction and marked osteoplastic changes especially involving the right half of the sacrum and contiguous portions of the ilium. The lumbar part of the spine and the lungs were negative for metastases.

The patient gradually lost weight and strength, and died on Aug. 11, 1923.

CASE 3.—S. T., a woman, was admitted to the hospital on Feb. 26, 1924. She had a combined Kraske operation in May, 1921, for an adenocarcinoma of the rectum with colloid degeneration. The patient was delivered of a normal child, in February, 1923. In August, 1923, active tuberculosis of left upper lobe developed. The patient was sent to Bedford Sanitarium on March 22, 1925. There were pain in the rectum, blood in the stools and diarrhea. In May, both gluteal regions were involved by carcinomatous tissue.

Roentgenograms of the pelvis taken on April 26, May 29 and September 11 were negative for metastases. Roentgenograms of the skull on Feb. 17, 1926, showed no metastases. The patient died on May 23.

At autopsy, colloid carcinoma of the rectum and metastases to the ribs and vertebrae were revealed. All ribs showed extensive tumor infiltration; in places they were swollen to twice their normal thickness. Metastases to subcutaneous and muscular tissues of the back, lungs, liver, kidneys, peritoneum, suprarenals, skin, brain and heart were found. There was obstruction of the left ureter with hydro-ureter and hydronephrosis. Pulmonary tuberculosis was revealed.

CASE 4.—W. B., a man, aged 61, was admitted to the hospital on Aug. 7, 1926. Three years before admission, the patient had blood in stools, had lost

weight and was weak. In 1924, colostomy was done and later a vesicocolonic fistula was made to relieve vesical obstruction.

On examination, the patient presented an enlarged liver and enlarged, hard inguinal glands. Over the anterior part of the chest, there was an "encurasse" of the tissues. A stony hard induration around the external sphincter prevented insertion of even the little finger. On Sept. 1, 1926, the patient suffered a spontaneous fracture of the right humerus.

The roentgen rays showed a pathologic fracture at the middle third of the shaft with an extensive area of bone destruction about 6 cm. in length at the site of the fracture. A roentgenogram of the chest showed pulmonary metastases. The patient died eight days later.

Autopsy revealed: carcinoma of the rectum with metastases to the regional lymph nodes, lungs, liver, kidney, suprarenals and skeleton; pathologic fracture of the right humerus; an irregular, flat elevation, 2 by 3 cm., on the lateral surface of the fourth right rib, adherent to a large mass on lateral surface of right middle lobe; tumor nodules on the inner surface of several ribs. These nodules were not adherent to the lung.

Case 5.—J. B., a man, aged 50, was admitted to the hospital on Jan. 22, 1927. One year previously, he had complained of abdominal cramps. In July, 1926, he had severe pain in the lower part of the back. Hemorrhoidectomy was performed. In September, he had a rectal hemorrhage, accompanied by weakness and loss of weight. Colostomy was done in October.

Physical examination revealed a ridge of hard, immovable tissue extending from the anus along the perineum. Three centimeters from the anal orifice, the rectal circumference was involved by firm tissue, and 6 cm. from the anal orifice, the entire rectal lumen was obstructed. The left eighth, ninth and tenth ribs were prominent and tender. Roentgenograms of the skull and chest were negative for metastases. The patient died on March 6, 1927.

Autopsy revealed adenocarcinoma of the rectum with metastases to the regional lymph nodes, liver, lungs, ribs and suprarenals. The right eighth and left sixth ribs were invaded by metastatic tumor nodules.

Case 6.—H. B., a man, aged 47, was admitted to the hospital on Jan. 15, 1928, with the history of having blood in the stools and rectal pain three years previously. Two years before admission, carcinoma of the rectum was diagnosed and colostomy done. In September, 1927, pain in the left leg developed. This pain was thought to be due to the enlarged inguinal glands, and they were given considerable roentgen therapy. A roentgenogram of the pelvis in October, 1927, was negative for metastases.

Physical examination on admission revealed a hard, moderately tender swelling over the middle of the left thigh about 8 cm. in diameter and attached to the bone. The left inguinal glands were enlarged and tender. Rectal examination revealed two large tumor tabs protruding from the anus, with numerous firm nodules in the rectum extending as high as could be reached.

A roentgenogram of the chest in January, 1928, was negative for metastases. A roentgenogram of the left femur taken in January, 1928, showed a thickening of the periosteum and a moderate amount of bone absorption in the middle third of the shaft. In April, 1928, roentgenograms showed an increase in the bone destruction of the left femur with invasion of the soft parts by a tumor mass extending to the inner and outer side of the shaft. Roentgenograms of the spine, pelvis, skull and humeri were negative for metastases. The patient died on June 15.

Autopsy revealed a colloid small cell carcinoma of the rectum with metastases to the retroperitoneal lymph nodes and inguinal glands, skin, liver, gallbladder and

left femur. The mass around the left femur stripped freely from the bone, but the cortex of the femur was thickened, finely nodular and of increased density. A segment of bone was not removed. The tumor mass had a gelatinous appearance, and through this portion were scattered numerous spicules of bone.

CASE 7.—N. S., a man, aged 63, was admitted to the hospital on June 10, 1928, with a history of pain in the rectum, mucous rectal discharge and diarrhea for six months. A colostomy had been done eight weeks prior to admission, and biopsy at that time showed a malignant adenoma. The patient had complained of a pain in the back for four weeks.

Examination revealed a large, hard mass completely obstructing the rectum. A roentgenogram taken on June 12 showed an irregular area of bone absorption in the upper end of the right femur, characteristic of early metastatic growth. The patient died on September 9 of a rectal hemorrhage.

Autopsy revealed a colloid carcinoma of the rectum with hemorrhage metastases to the regional lymph glands and liver. The femur was not examined.

CASE 8.—E. C., a woman, aged 68, was admitted the hospital on Jan. 8, 1930, with a history of having had a sacral Kraske operation performed two years previously for adenocarcinoma of the rectum with lymph nodes involved. The patient remained in good health for one year following operation, and then pain in the rectum developed. Two months before admission she noticed a lump on the back of her head.

Examination showed a large circumscribed cystic tumor over the occipital region with a hard nodule in front of it. On January 17, the roentgen rays disclosed areas of bone destruction in the right half of the occipital bone and the posterior portion of the right parietal bone. These areas were characteristic of metastatic deposits. The pelvis, femora and humeri were negative for metastases. There were some thickening and narrowing of the artificial anus, but no definite local recurrence could be felt. The patient was discharged on February 12, to be followed in the outpatient clinic.

COMMENT

In five of these eight cases, the presence of the skeletal metastases was proved by autopsy. In another, autopsy was performed, but the site of the metastasis could not be investigated. In the three cases not proved by autopsy, the roentgen-ray observations were sufficiently typical to make a positive diagnosis. In six cases, the diagnosis was made clinically, and in the remaining two the secondary growths were not discovered or suspected until after death. In practically all of these eight cases, as well as in most of those reported in the literature, the disease was of long standing, and as carcinoma of the rectum is known to spread slowly, even locally, it is not surprising to find the skeletal metastases occurring late in the course of the disease.

The site of metastases is of interest, because in the entire twenty-four cases the various bones are involved with practically the same frequency as originally described by von Recklinghausen [17] in his monograph on the formation of bone metastases. The skeleton was the site of

17. von Recklinghausen, F. D.: Festschr. der Assistenten zu Virchow zu 71st Geburtstag, Berlin, 1891.

metastases thirty-five times in these twenty-four cases. The frequency and percentages were as follows:

Vertebrae	8	22.8%
Femur	6	16.8%
Ribs	6	16.8%
Skull	3	8.4%
Sternum	3	8.4%
Humerus	2	5.7%
Pelvis	2	5.7%
Sacrum	2	5.7%
Radius	1	2.8%
Scapula	1	2.8%
Ulna	1	2.8%
	35	

Von Recklinghausen claimed that metastases to the bone are not due to the embolic blocking of a vascular channel in the bone by a large mass of malignant cells, but are caused by the periaxial stagnation of the neoplastic cells as they pass from the blood vessels outside of the bony structure into the vascular bed situated within the bone. The blood vessels around the bone are of changeable size, depending on stimuli such as temperature and activity, while the vessels within the bone are of fixed caliber. In this manner the blood is often carried from a narrowed peripheral vessel into a wider vessel within the bone-marrow. This change in size of the vascular bed would tend to stagnate the neoplastic cells and to favor their multiplication. After they had multiplied sufficiently, they would block the vascular channel and then extend outward to the periosteum through the foramina without necessarily eroding the cortex.

Owing to this manner of formation, bone metastases should occur most frequently in those bones subject to the greatest strain and stress as well as to changes in temperature. Von Recklinghausen claimed that according to this theory, the frequency of bone metastases in various parts of the skeleton would be as follows: vertebrae, femur and pelvis, ribs and sternum, humerus, skull, tibia, radius and ulna. Practically all statistics have in the main confirmed his original contention. Nisnjewitsch,[1] in 169 metastases to the bone, found the following frequency: vertebrae, 28.9 per cent; sternum, 17.7 per cent; femur, 15.9 per cent; ribs, 14.7 per cent; humerus, 7.6 per cent; skull, 7.1 per cent; pelvis, 5.3 per cent; tibia, 1.1 per cent; clavicle, 1.1 per cent.

The importance of the clinical diagnosis of bone metastases is shown in cases 4 and 6. In case 4, a pathologic fracture might have been prevented if the presence of considerable destruction of the bone had been recognized. In case 6, for a number of months, the pain in the leg

was considered to be due to the enlarged inguinal glands, which were given roentgen therapy. As irradiation offers some relief from pain in these skeletal metastases, their occurrence should be kept in mind, and all pains in the bone investigated by means of the roentgen ray.

SUMMARY

1. A series of eight cases of rectal carcinoma complicated by skeletal metastases is added to the sixteen reported in the literature.

2. In the main, the site of the metastases conforms to the original table of frequency as stated by von Recklinghausen.

3. Metastases to the bone in carcinoma of the rectum occurs late in the course of the disease, but with sufficient frequency to make it of clinical significance and to make its early diagnosis of great importance in relief from pain and the prevention of fractures.

THE VALUE OF DRUGS IN THE RELIEF OF ILEUS

AN EXPERIMENTAL STUDY *

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NEW ORLEANS

The classification of cases of ileus into mechanical and paralytic varieties or, according to a different terminology, dynamic and adynamic varieties, is a distinction of fundamental importance. The mechanical or dynamic variety, by definition, is characterized by some condition which physically prevents the normal progress of intestinal contents toward the anus. The relief of such a physical obstruction is essentially a surgical matter involving relief of intestinal kinking, division of bands of adhesions, removal of new growths, circumvention of constrictions by accessory openings between adjacent intestinal loops or other surgical procedures, according to the indications presented by the individual case. If the patient with such an obstruction comes to operation early, this purely surgical therapy is all that is required. In the paralytic or adynamic ileus, however, a different state of affairs exists. There may or may not be some physical hindrance to the passage of intestinal contents along the intestinal canal, depending on whether the ileus was paralytic from the beginning or developed on the basis of a preceding dynamic ileus. If the mechanical factor is still present, this, of course, must be overcome as a prerequisite to success in the treatment for the paralytic condition, but the relief of a mechanical ileus associated with a paralytic ileus is, of course, of no value in itself. The fundamental abnormality, at least in the early stages before profound toxemic and physicochemical changes have occurred, is one involving the contractility of the muscular tunics of the involved segment of intestine. Although restoration of normal motility to a segment of paralyzed intestine may or may not save the life of the patient, he certainly will not recover unless this state of affairs can be established. There is considerable evidence to support the view that patients suffering from intestinal obstruction may live for a considerable number of hours in spite of the fact that inevitably fatal organic or physiologic changes

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have already developed. In this connection it is exceedingly significant that not infrequently patients with advanced paralytic ileus succumb promptly as soon as the ileus is relieved. Indeed, clinicians of experience do not view the resumption of peristalsis in an intestine that has been paralyzed for a considerable period of time with entire equanimity, since the patient may either become worse and die or may rapidly become improved and survive, depending probably on the amount of toxin previously absorbed, and the clinician has no available means of determining which direction the subsequent course of events may pursue. In any case, there is every reason for believing that any measure designed to restore movement to a paralyzed intestine will ordinarily be of value more or less directly in proportion to the promptness with which it is invoked. Perhaps it is hardly necessary to emphasize in this way the fundamental gravity of paralytic ileus, but in this paper we deal primarily with the value of drugs in the treatment for this type of ileus.

It is a matter of common knowledge that drugs, as a rule, are of relatively little value in combating the well established and graver forms of disease processes in general. It would seem in order, therefore, to emphasize the fundamental importance of the early recognition and early treatment for any abnormal process in which reliance is to be placed on drug therapy. In the following discussion of the usefulness of drugs in the treatment for paralytic ileus, all clinical and experimental evidence is considered solely in its relation to the case that has been recognized early. A large part of the experimental evidence about to be cited has been derived from observations on the behavior of normal or, at least, relatively normal musculature, and it would be gratuitous to assume that the reactions observed, when dealing with normal or relatively normal muscle, are directly applicable to muscle that has been subjected to the changes incident to prolonged paralytic ileus. It should hardly be necessary to remark that the relief of ileus is not synonymous with the treatment for ileus, since the treatment for ileus involves not only restitution of normal movement to the intestinal tract, but also the combating of any associated abnormal process that may occur in connection with the paralysis. In this treatise we are concerned solely with a consideration of the use of drugs frequently considered beneficial in the stimulation of intestinal motility, drugs which presumably may be of value in restoring normal motility to a paralyzed intestine.

METHODS AVAILABLE FOR THE DETERMINATION OF THE ACTION OF DRUGS ON INTESTINAL MOTILITY

A number of different methods have been employed in testing the action of various drugs on intestinal motility.

The first and most fundamental of these involves the direct action of the drug on isolated portions of the intestinal musculature, arranged

after the manner of the "Magnus" or "Trendelenburg" preparation. Usually the isolated strip of muscle has been immersed in an artificial blood serum like Locke's, Ringer's or Tyrode's solution to which a small amount of the test drug has been added. The effect on motility is recorded on a kymographic drum by means of a system of levers.

A second method, which is really a modification of the first, takes into consideration not only the muscular tissue as such, but also its intrinsic nerve supply, i. e., the plexuses of Auerbach and Meissner. The method is essentially the same as the first, except that instead of muscle alone, strips of muscular tissue which retain their intrinsic nerve supply are used. The two foregoing methods are obviously open to criticism in that the conditions involved are artificial. However, they have the advantage that they tend to reduce the number of experimental variables to a minimum.

A third method, and a much more physiologic one, makes use of an intact animal with a so-called Thiry or Thiry-Vella fistula. In this type of fistula a loop of intestine is isolated by transverse incisions made at some distance from one another, and the severed ends are stitched to the abdominal wall, making a permanent communication between the lumen of the segment and the body surface; continuity of the gastrointestinal tract is then restored. The loop of intestine thus isolated is made the subject of experimentation. The method has the advantage of preserving intact the nerve and blood supply to the loop of intestine under experimentation, but is unphysiologic in that the loop does not maintain its physical continuity with the intestinal tract. In determining the effect of drugs on intestinal motility, a balloon has ordinarily been placed within the lumen of the isolated segment, and intestinal motility has been recorded in the form of a tracing on the kymographic drum.

A fourth method consists in the observation of intestinal movement by means of the fluroscopic screen. This method is more physiologic than the preceding one, but it is subject to two disadvantages: 1. An opaque substance must be present within the lumen of the intestine in order that a recognizable shadow may be produced. 2. The outline cast by the opaque material on the fluoroscopic screen is, at best, somewhat indistinct, and, therefore, subject to misinterpretation. Incidentally, the personal equation introduced by the observer himself must be considered, as the method does not ordinarily permit the taking of reliable objective records.

A fifth method, if indeed it may be called a method at all, is that of the observation of clinical cases. The presence of borborygmi on auscultation of the abdomen and the appearance of flatus and feces at the anus are taken as presumptive evidences of intestinal motility. Although this method is the most physiologic of all, it is also the most unscientific. So many variables are present and the personal equation

is of so great importance that observations made when using such a method may be untrustworthy.

A variation of the last method, which may conveniently be designated as a separate or sixth one, is the unaided ocular observation of the open abdomen either of experimental animals or of patients. The method is open to the same criticism as the last method with respect to the personal equation in addition to the criticism that the subject being subjected to study is under abnormal conditions.

A seventh method, the one that we have used in our experimental investigations, consists of laparotomy under a general anesthetic and the recording of intestinal movement by means of a balloon introduced into the intestinal tract at the time of or, at least, just preceding the investigation itself. This method is open to criticism: (1) because the observations must of necessity be made under some form of anesthesia or analgesia; (2) because of unavoidable injury to the intestinal tract incident to the insertion of a recording device into the lumen of the intestine, and (3) because of the abnormality incident to the opening of the abdomen and consequent changes in pressure relationship and other physical influences. The last criticism may be overcome to a certain extent by opening the abdominal cavity within a bath of warm physiologic solution of sodium chloride, and the second criticism may be minimized, though not obviated, by gentleness and care in the use of the apparatus.

TECHNIC ADOPTED BY THE AUTHORS

Many different animals have been used by other investigators as subjects for experimental observation: rabbits, dogs, cats, guinea-pigs, rats and frogs. Our own observations have been made exclusively on dogs. Dogs are particularly suitable for use in experiments on intestinal obstruction, because in their intestinal reactions they simulate, more nearly than most other animals, the reactions observed in the human subject. Many of the other common laboratory animals present fundamental organic differences in structure from those found in man, and in any case many of them are too small to be conveniently used according to the technic adopted by us. The cat has been used somewhat extensively in experimental investigations of intestinal motility, especially by Cannon and his co-workers,[1] but this animal is unduly resistant to the production of intestinal obstruction, and it is doubtful whether experimental results obtained by using such material would be directly applicable to cases in human beings. The rabbit, another animal frequently used in experiments on ileus and also for purposes of determining the action of drugs on intestinal motility, is a particularly

1. Cannon, W. B., and Murphy, F. T.: Physiologic Observations on Experimentally Produced Ileus, J. A. M. A. **49**:840 (Sept. 7) 1907.

poor experimental animal for use in experiments involving the observation or recording of movements of the gut. This animal, in addition to presenting anatomic peculiarities characteristic of the herbivorous animals, also presents a hyperactive intestine, and the ileus which is characteristically seen in many other animals including man, as the result of simple opening of the abdomen, is not seen in rabbits, the intestinal movement continuing in apparently uninterrupted fashion for minutes or even hours after laparotomy has been performed and frequently continuing for long periods even after the death of the animal had ensued. Experimental observations made on as excitable an organ as the intestinal tube of the rabbits would seem to be of relatively little value in their application to the human intestine.

Six-three animals were used in the experiments to be reported, and the following drugs were employed: pituitary extract, physostigmine, peristaltin, pitocin, choline, acetyl choline and hypertonic sodium chloride solution. The method of procedure was as follows: The dogs were usually anesthetized with sodium barbital introduced by stomach tube, from 0.25 to 0.3 Gm. of the drug per kilogram of body weight being introduced in warm watery solution. When the animals had become anesthetic, as they did after a period of from one to three hours, the abdominal wall was incised to the peritoneum, care being taken to insure hemastasis, but the peritoneum itself was not disturbed. A midline incision was made in the neck and the trachea; the common carotid artery and the external jugular vein were exposed and isolated. The dog was then completely immersed, except for the head and neck, in a bath of saline solution heated to from 38.6 to 40 C. The temperature of the bath was maintained at this level throughout the experiment. A cannula was next introduced into the trachea, and connections were made between it and a recording tambour. The carotid artery was next cannulated, and by a system of rubber tubes filled with 2 per cent sodium citrate solution connections were made to a mercury manometer provided with a rider, lever and writing point. The external jugular vein was left exposed for the injection of the various drugs by hypodermic syringe and needle. The peritoneum of the animals was then incised, and a loop of ileum near the ileocecal junction was carefully withdrawn. This intestinal loop was manipulated under water. A purse-string suture was placed in the wall of the bowel at its antimesenteric border, and a rubber tube terminating in a thin-walled rubber balloon was introduced for a short distance into the lumen of the intestine through an incision placed within the purse-string suture. The purse string was then tied tightly about the rubber tube. This rubber tube was connected to a tambour and writing point; a rubber bulb was provided by which air could be introduced into the intestinal balloon to produce any desired degree of initial pressure. In certain of the experiments normal animals were used, but in other experiments, animals in which experimental obstruction had been performed previously; the production of this artificial mechanical ileus was always made to precede the experimental observations by a period of forty-eight hours. For the production of obstruction, the abdomen of the animal was opened under ether anesthesia by means of a small low right rectus incision. The terminal ileum was located and was encircled by a piece of umbilical tape, the tape being tied sufficiently tightly to effect complete closure of the intestinal lumen, but not sufficiently tightly to produce strangulation of the intestine at this point. In a number of animals in which the tape was tied too tightly, the animal succumbed

to perforation and generalized peritonitis. The obstructed loop of intestine was replaced within the abdomen; the abdominal wound was sutured in layers, and the animal was allowed to recover. This procedure was, of course, performed under strictly aseptic conditions.

Using the technic previously described, tracings of the respiratory rate, the blood pressure and the intestinal movement were all obtained on a relatively narrow strip of kymographic paper. A long paper kymograph was used, and the drum was adjusted to revolve at a relatively low rate of speed so that observations could be continued over considerable periods of time, viz., from two to three hours. In certain of the experiments three balloons were inserted into the gut instead of one, the first balloon being inserted into the duodenum, the second into the ileum and the third into the colon. In the case of the animals that had undergone previously obstruction with tape, an additional opening was usually made into the terminal ileum, and a catheter was introduced in order to permit decompression of the dilated and fluid-filled intestine at that point and also to permit of observations on the efficiency of the various agents in actually extruding fecal material from the intestinal lumen.

Certain control experiments not specificially mentioned were made under ether anesthesia and others under local infiltration analgesia.

REVIEW OF THE LITERATURE

The Action of Pituitary Extract.—Oliver and Schafer [2] are given credit for having introduced extracts of the pituitary gland into the practice of medicine by their demonstration of the action of extracts of this gland on smooth muscle. Largely because of the admitted stimulatory influence of pituitary extract on the smooth muscle of the uterus, it has been assumed that it has a similar effect on the smooth muscle of the gastro-intestinal tract, though this assumption has never been universally accepted. Bayer and Peter [3] found that extracts of the posterior lobe of the pituitary gland usually caused a stimulation of excised rabbit's gut after a preliminary period of inhibition. Houssay,[4] in 1922, was able to corroborate this observation on excised rabbit's gut as far as the stimulatory action of extract of the posterior lobe was concerned. In certain cases, however, he obtained inhibitions of intestinal movement, which he interpreted as being due to the action of chloretone contained in commercial preparations of the drug. He expressed the belief that chloretone-free preparations always act as stimulants. King and Church,[5] in 1923, using isolated preparations from the muscularis mucosae, found that when pituitary extract was applied to "cylinder" preparations, it caused definite shortening of the tissue, an effect which they had never been able to obtain by injecting pituitary

2. Oliver, G., and Schafer, E. A.: J. Physiol. **18**:277, 1895.

3. Bayer, G., and Peter, L.: Arch. f. exper. Path. u. Pharmakol. **64**:204, 1911.

4. Houssay, B. A.: Acción fisiológica de los extractos hipofisiarios, Buenos Aires, 1922.

5. King, C. E., and Church, J. G.: Am. J. Physiol. **66**:428, 1923.

extract into living animals. Cross,[6] using isolated pieces of the appendix taken from human patients at operation and suspended in Locke's solution at a temperature of 37 C., found that the addition of 0.5 cc. of pituitary extract to the solution produced a slight increase in tone in the musculature. Kaufmann,[7] in 1927, using a histamine-free preparation and one that did not contain chloretone, found that concentrations of pituitary extract varying from 1:10,000 to 1:100,000 had no effect either on the duodenum or on the jejunum; however, such concentrations caused a definite stimulation of the ileum in both cats and rabbits. The effect consisted of a definite increase in tone as well as an increase in the pendular movement and an increase in the frequency of this movement.

In the case of the colon, concentrations of from 1:250,000 to 1:1,000,000 frequently produced a typical effect characterized by a preliminary phase of inhibition of tone and cessation of pendular movement, soon followed by a definite increase in tone and an increase in pendular movement. Uno [8] found that a chloretone-free preparation of the posterior lobe of the pituitary gland had an inhibitory action on pendular movement and tone in the excised gut of the rat. McIntosh and Owings,[9] in 1928, working with animals subjected to experimentally produced intestinal obstruction and measuring the intra-intestinal tension by means of a special apparatus introduced into the gut, found that freshly prepared pituitary extract invariably showed a relaxing rather than a contracting effect on the intestinal musculature. Brunner and Weigand [10] observed under the fluoroscope the large bowel of cats to which a barium sulphate enema had been given. Pituitary extract was thought to be of little value in the stimulation of colonic movement. Garry,[11] in 1927, found that only exceptionally was stimulation of the small bowel of the guinea-pig produced by injection of the extract of the posterior lobe or of the pars intermedia of the pituitary, and, when stimulation was produced, it was but temporary.

Concentrations of the drug of 1:1,000 or more characteristically produced inhibition of peristalsis, which was of long duration. Ross,[12] in 1926, using a rubber balloon introduced into the intestinal lumen of a normal experimental animal, found that pituitary extract frequently

6. Cross, D. G. T. Kerr: Brit. M. J. **1**:9, 1924.

7. Kaufmann, Margot: Arch. f. exper. Path. u. Pharmakol. **120**:322, 1927.

8. Uno, T.: Am. J. Physiol. **61**:203, 1922

9. McIntosh, C. A., and Owings, J. C.: The Effect of Solutions of Pituitary and Various Drugs on the Movements of the Small Intestine During Simple Mechanical Obstruction, Arch. Surg. **17**:996 (Dec.) 1928.

10. Brunner, T., and Weigand, W.: Klin. Wchnschr. **8**:1115, 1929.

11. Garry, R. C.: Arch. f. exper. Path. u. Pharmakol. **120**:348, 1927.

12. Ross, J. W.: Canad. M. A. J. **16**:241, 1926.

failed to produce any motor response in the gut. Voegtlin and Dyer,[13] using rats as experimental animals, found that in chloretone and histamine-free preparations of extract of the posterior lobe both tone and pendular movement were inhibited. Dixon,[14] in 1923, found that although extracts of the posterior lobe of the pituitary caused stimulation of the small intestine, an inhibitory action was produced in the colon. MacDonald,[15] in 1925, stated the belief that although the action of extracts of the posterior lobe of the pituitary gland is essentially stimulatory to the intestinal musculature, this action is due especially to contamination with histamine, and that if this is removed, the stimulating action of the drug is largely destroyed. Ross [12] found pituitary extract stimulating to rabbit's gut, and expressed the belief that when this effect is not seen, contamination with chloretone is responsible. Degener [16] observed a characteristic inhibitory action of extract of the posterior lobe of the pituitary gland on the pendular movement of the small intestine in the rat. Guggenheim,[17] in 1914, found that pituitary extract produced stimulation of excised rabbit's gut, but that, however, if alkalis were added to the extract, the stimulating effect was not destroyed; the stimulating effect on the uterine musculature, however, was destroyed by this procedure.

Clinical reports on the efficacy of pituitary extract in the treatment for intestinal obstruction are rather abundant. Blair Bell [18] was among the first to make use of and advocate the use of pituitary extract clinically for its effect on the intestinal musculature. Bidwell [19] reported favorably on the routine postoperative use of pituitary extract for its effect on peristaltic activity. For adults he advocated the use of 1 cc. six hours after operation, the dose to be repeated every four hours until eighteen doses had been given. He credited this therapy with favorable results—the early passage of flatus, marked absence of abdominal discomfort and satisfactory action of the bowel after the administration of an enema. This report, of course, comes from the period in surgery when the early resumption of intestinal activity was considered a clinical desideratum, and the surgeon became worried unless there was a copious bowel movement within the first twenty-four

13. Voegtlin, C., and Dyer, H. A.: J. Pharmacol. & Exper. Therap. **24**:101, 1925.

14. Dixon, W. E.: J. Physiol. **57**:179, 1923.

15. MacDonald, A. D.: Quart. J. Exper. Physiol. **15**:191, 1925.

16. Degener, L. M.: Am. J. Physiol. **60**:107, 1922.

17. Guggenheim, M.: Biochem. Ztschr. **65**:189, 1914.

18. Bell, Blair: Brit. M. J. **2**:1609, 1909.

19. Bidwell, L. A.: Investigation into Effect of Pituitary Extract on Bowels after Abdominal Operations, Clin. J. **38**:351 (Sept. 6) 1911; abstr., J. A. M. A. **57**:1242 (Oct. 7) 1911.

hours postoperatively. Duffey,[20] reporting from the same general period as the preceding author, stated that pituitary extract was used with favorable results in ten cases of postoperative stasis. It was the customary routine of this author to cause the patient's bowel to move within thirty-six hours after operation by the use of mild mercurous chloride and within forty-eight hours by the use of an enema. His advocacy of the method is dependent on his observation that the bowels would frequently move with the aid of pituitary extract, when they would not by routine methods.

Mayer,[21] in 1924, reporting on the use of pituitary extract in the treatment for postoperative ileus, reported fifty-two cases, in thirty-six of which the injection of the drug was followed by defecation and the passage of flatus. Vogt,[22] reporting on the results of pituitary extract and intravenous salt solutions combined in the treatment for intestinal obstruction, stated that when this therapy is used favorable results are seen in that the pulse rate becomes slower and stronger, the blood pressure becomes increased, and usually within the course of from five to seven minutes the patient feels uncomfortable in the region of the abdomen and soon thereafter evacuates both gas and feces. He stated that pituitary extract affects the entire intestinal tract, and this he believed to be a factor of value in the treatment which he recommended. He considered that the saline solution is of value merely in diluting and causing the excretion of the toxin. He reported the recovery of fifteen patients in a series of eighty-one cases, a percentage of 22.2. He expressed the belief that if the intestinal tract does not respond to the use of hypophysin, the intestine is in a state of complete paralysis. Krinsky,[23] in 1927, reported a severe case of ileus secondary to peritonitis, in which the pituitary-saline infusion of Vogt was believed to have saved the patient's life.

The Action of Physostigmine.—Physostigmine is the active principle of the calabar bean. Physostigmine has been used clinically for its action on the intestinal tract for nearly fifty years. Fröhner[24] is authority for the statement that physostigmine was originally used in veterinary surgery in the treatment for ileus in animals, for instance in colic, by Dieckerhoff in 1882. Westermann[25] reported the occurrence of tetanic contraction of the intestinal wall in cats, rabbits and dogs in

20. Duffey, R.: New York M. J. **101**:72, 1915.
21. Mayer, A.: München. med. Wchnschr. **71**:931, 1924.
22. Vogt, E.: München. med. Wchnschr. **73**:1509, 1926.
23. Krinsky, A., and Stein, E.: Zentralbl. f. Chir. **54**:591, 1927.
24. Fröhner, E.: Toxikologie für Thierärzte, ed. 2, Stuttgart, Ferdinand Enke, 1900.
25. Westermann, W.: Untersuchungen über die Wirkungen der Calabarbohne, Dorpat, 1867.

from eight to ten minutes after the administration of 2.5 per cent glycerin solution of the alcoholic extract of the calabar bean and offered the hypothesis that this effect was due to stimulation of the sympathetic ganglions in the intestinal wall. Alvarez,[26] working with excised segments of rabbit's gut, observed that physostigmine, as well as certain other drugs, increased the tone of the musculature of the intestinal wall from the duodenum to the colon, whereas pituitary extract, which has been considered previously, characteristically presented a depressant effect on the rate of contraction. Cross,[6] using segments cut from the appendix removed at operation from human patients, found that physostigmine, when exhibited after pituitary extract, produced a very definite increase in the muscular tone, the pituitary extract itself producing only a slight increase. When the same two drugs were employed in the reverse order, there was relatively little effect. The use of pituitary extract following physostigmine produced only a relatively slight increase in tone. Baur,[27] using a Trendelenburg preparation and physostigmine salicylate, found that this drug produced little change in the tone of the intestinal musculature, but produced marked increase in the amplitude of peristalsis, especially in the longitudinal muscle fibers. On the basis of differences in action between the longitudinal and circular muscle responses, he expressed the belief that the action of the drug consists in increasing or changing the irritability of Auerbach's plexus. Ludlum and McDonald,[28] in 1926, found in one clinical case that the administration of $\frac{1}{64}$ grain (0.00101 Gm.) of physostigmine sulphate twice a day for six days produced a markedly contracted state of the colon, as shown on the fluoroscopic screen. LeHeux,[29] in 1921, working by the roentgenographic method, found that physostigmine produced cramplike contractions of the gastro-intestinal tract.

Brunner and Weigand,[10] working by the fluoroscopic method and using cats, found that the exhibition of physostigmine produced a lively movement in the intestinal tract of these animals, which within from twenty to forty minutes resulted in active defecation. Oppenheim,[30] working with rabbits and dogs, inflated the bowel through the rectum, opened the abdomen, made a small opening in the colon and then injected 0.003 Gm. of physostigmine salicylate. Immediately following the injection, feces and gas were expelled from the colostomy opening. Twenty minutes after the injection the maximum action of physostigmine had been attained, and the action of the drug was found to last from one half to three quarters of an hour. Baur,[27] working with the

26. Alvarez, Walter C.: Am. J. Physiol. **46**:554, 1918.
27. Baur, M.: Arch. f. exper. Path. u. Pharmakol. **131**:233, 1928.
28. Ludlum, S. D., and McDonald, E.: M. J. & Rec. **123**:228, 1926.
29. LeHeux, J. W.: Arch. f. d. ges. Physiol. **190**:301, 1921.
30. Oppenheim, A.: Deutsche med. Wchnschr. **28**:226, 1902.

alcoholic extract of the calabar bean in cats, found that the drug produced a marked spasmodic contraction of the entire gastro-intestinal tract from the stomach to the rectum, with the production of watery evacuations mixed with blood and mucus. Ross,[12] using experimental animals and a graphic method involving the introduction of a rubber balloon into the intestine, found that physostigmine was of greater value than pituitary extract in the stimulation of intestinal movement, but he regarded even physostigmine as a relatively valueless drug. Traversa,[31] in 1899, working on the pharmacologic action of physostigmine, stated that the action of this drug on the intestinal tract is not modified by the exclusion of the medulla, the vagus and sympathetic nerves or the celiac ganglion. The contractions produced by the drug could be prevented or stopped, however, by the administration of atropine. Cannon and Murphy,[1] in 1907, injected physostigmine into animals in which ileus had been produced by crushing the testicle of the animal while under general anesthesia. Although in their experience the inhibition of the drug resulted in no hyperperistalsis in a normal animal, it produced a definite, though temporary, increase in peristalsis in animals so treated. Heller,[32] in 1883, reported the use of the calabar bean in combating constipation and flatulence due to atony of the intestines. Clinical cases showed favorable effects. Subbotin [33] used the extract of calabar bean and also the extract of *Physostigma* with good results in cases of atony of the bowel. Schaefer,[34] in 1880, reported good results from the use of the calabar bean in five cases of chronic constipation and flatulence. In the earlier years of the present century, a number of authors used physostigmine salicylate both as a prophylactic and as a curative measure in the treatment for postoperative ileus. As previously stated, early postoperative evacuation of the bowel was considered desirable or almost necessary at that time. Noorden,[35] in 1901, reported favorably on the use of physostigmine, repeated at intervals in diminishing doses and beginning with 0.5 mg. Packard,[36] in 1902, reported a case of copious intestinal evacuation as the result of the injection of $\frac{1}{150}$ grain (0.001 Gm.) of physostigmine salicylate, which was repeated in two hours; this was in a case of intestinal obstruction. In 1904, Packard [36] recommended the injection of 0.001 Gm. of physostigmine sulphate immediately postoperatively. He expressed the opinion that the action of the drug persists for three or four hours. The beneficial results obtained from the use of the drug were absence of distention and

31. Traversa, G.: Policlinico **5**:1, 1898.
32. Heller, A.: Deutsche med. Wchnschr., 1883, p. 123.
33. Subbotin: Deutsches Arch. f. klin. Med., 1869, p. 284.
34. Schaefer, S.: Berl. klin. Wchnschr. **17**:725, 1880.
35. Noorden, C.: Berl. klin. Wchnschr. **38**:1057, 1901.
36. Packard, F. A.: Philadelphia M. J. **9**:929, 1902.

passage of gas by bowel within a very few hours of the completion of the operation. Arndt,[37] in 1904, reported five cases in which the injection of physostigmine salicylate was apparently of life-saving value, and stated that he had never seen this drug fail in the treatment of patients with ileus, except in cases due to acute bacterial peritonitis. Vogel,[38] in 1904, reported favorable results following the routine injection of 0.0004 Gm. of physostigmine given to patients soon after operation; during three years he saw no cases of ileus. In cases of intestinal adhesions, he recommended the injection of physostigmine while the patient was still on the operating table. He expressed the opinion that this method was of prophylactic value in the prevention of recurrent adhesions. Craig,[39] in 1904 and 1905, warmly advocated the prophylactic use of physostigmine in the prevention of postoperative ileus, especially in the prevention of postoperative ileus due to adhesions. Góth,[40] in 1908, reported the cases of three patients with ileus treated successfully by the administration of physostigmine at a time when they were apparently moribund. Moenninghoff [41] warmly recommended the prophylactic use of physostigmine in the prophylaxis for distention following laparotomy. He gave 1/40 grain (0.001 Gm.) of the drug immediately following operation and followed this with an enema, because he believed that physostigmine acts only on the small bowel. Martzloff,[42] in 1924, in a clinical report from the Johns Hopkins Hospital, said that he found the prophylactic administration of physostigmine salicylate in a dose of 0.01 Gm. and strychnine sulphate in a dose of 1/40 grain (0.001 Gm.) given hypodermically of little or no value in the prophylaxis of postoperative complications. He reported the cases of 162 patients observed during a period of eleven months, all of whom had been subjected to major abdominal operations under ether anesthesia. The series of cases is well controlled in that alternate cases received drug therapy. He concluded that distention, gas pains and emesis occur more frequently in patients treated thus than in a similar series of untreated patients. Voluntary micturition was also established earlier in the nontreated than in the treated patients. Martin and Weiss [43] reported favorably on the use of physostigmine in the treatment for abdominal distention. Their clinical observations led them to believe

37. Arndt, Gustav: Zentralbl. f. Gynäk. **28**:273, 1904.

38. Vogel, K.: Zentralbl. f. Gynäk. **28**:699, 1904.

39. Craig, Daniel H.: Am. J. Obst. **49**:449, 1904.

40. Góth, L.: Zentralbl. f. Gynäk. **32**:1629, 1908.

41. Moenninghoff, F. J.: J. Missouri M. A. **5**:193, 1908.

42. Martzloff, K. H.: Bull. Johns Hopkins Hosp. **35**:370, 1924.

43. Martin, H. E., and Weiss, S.: The Use of Physostigmin in Abdominal Distention, J. A. M. A. **84**:1407 (May 9) 1925.

that the smallest single therapeutic dose that will afford relief is 2 mg., or 1/30 grain. The average dose which they employed was 4 mg., or 1/16 grain (0.004 Gm.). As high as 13 mg., or 1/5 grain, was administered to one patient. They administer the drug by the intramuscular route, and in from ten to forty minutes after the injection they found that the patient belches or expels gas from the rectum. This effect gradually increases in frequency, and the volume of gas expelled also increases; defecation characteristically occurs, sometimes accompanied by moderate colic. In a total of sixteen cases of abdominal distention following laparotomies, all of the patients were relieved from their symptoms by the injection of the drug. Vogel [38] recently, in 1928, reported good clinical results with the use of physostigmine.

The Action of Choline and Acetyl Choline.—In 1912, Weiland [44] made the accidental observation that when isolated strips of intestine were allowed to contract for considerable periods of time in Ringer's solution, the Ringer's solution when brought into contact with other pieces of intestine showed the property of producing excitation in them. The substance responsible for this reaction was isolated first in Magnus's laboratory, at Utrecht, by LeHeux.[29] Magnus [45] thought that he had isolated the hormone responsible for the regulation of intestinal activity, since it was found not to affect the uterus or heart but was specific for the intestinal musculature. This substance, called choline, is apparently derived from the intestinal musculature itself, and the intestine has been found to conserve its supply of the material. The first experiments with choline were performed in Magnus's laboratory, and it was found by fluoroscopic examination that paralysis of the intestine induced by prolonged chloroform narcosis was speedily relieved by the injection of from 5 to 15 mg. of choline per kilogram of body weight. Magnus [45] determined the safe intravenous dose in cats as 20 mg. of the substance per kilogram of body weight, and he found that when injected at a rate of 0.8 mg. per kilogram per minute large doses of the drug were tolerated. Holt and Grossman [46] stated that choline is normally present in the musculature of the stomach and the intestine. They said that the substance is not absent from the gut in ileus. Magnus,[45] in 1925, stated that choline activates the plexus of Auerbach, since, if the plexus is removed, much larger doses of choline are required to stimulate the muscle. He stated that the isolated small intestine of the rabbit gives off 3 mg. of choline from its serosal side during the course of an hour. This author [45] is authority for the statement that the choline content is almost invariably found to be normal in all cases save in morphine poisoning.

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44. Weiland, W.: Verhandl. d. Kong. f. inn. Med. **29**:165, 1912.
45. Magnus, R.: München. med. Wchnschr. **72**:249, 1925.
46. Holt and Grossman: München. med. Wchnschr. **72**:251, 1925.

Guggenheim and Loeffler[47] made quantitative analyses of the amount of choline in the blood and urine. They found that a liter of urine contained from 0.002 to 0.01 Gm. of choline hydrochloride, and that a liter of serum contained from 0.002 to 0.02 Gm. Choline has the formula trinethyloxyethylammonium hydrochloride. Dale,[48] in 1914, investigated the action of four different esters of choline: (1) the choline nitrous ester, the so-called synthetic muscarine of Schmiedeburg and Harnach; (2) the choline nitric esther; (3) the choline ethyl ether, and (4) acetyl choline. All four substances were found to be powerful stimulants to the musculature of the esophagus and stomach and to the small and large gut. In the intact animal, acetyl choline was found to be the weakest of the four drugs when injected intravenously; the other esters showed more powerful and prolonged action. On the isolated muscle, however, acetyl choline was somewhat more active than the other three. The explanation offered for this observation is that acetyl choline is very rapidly oxidized in an alkaline medium; the drug, when injected intravenously, reaches the heart relatively rapidly and affects it maximally, but it reaches the intestine only after considerable time has elapsed, during which oxidation has occurred. Dale[48] found that 0.000001 mg. of acetyl choline produced a definite decrease in the blood pressure of the cat. LeHeux[29] isolated acetyl choline, as well as choline, and acetyl choline was found to produce a reaction of the order of a hundred times as great as choline alone. LeHeux,[29] working in 1921 and experimenting on the choline esters of succinic, pyruvic, butyric, isovaleric and benzoic acids, found that the succinic ester of choline showed no greater effect than did choline alone. He gave the relative value of the various other esters as follows: The choline ester of acetic acid is 1,000 times as powerful an intestinal stimulant as choline itself; propionic acid, 300 times; formic acid, 100 times; butyric acid, 40 times; isovaleric acid, 15 times, and benzoic acid, twice.

Most authors accept the statement that acetyl choline is 1,000 times as powerful an intestinal stimulant as is choline, e. g., Wolf and Canney[49] and Magnus.[45]

Wolf and Canney[49] reported the effect of the injection of choline in four clinical cases, in three of which the injection was believed to have been of life-saving value. Arai[50] was able to relieve experimentally produced ileus in cats by the use of choline, ileus having been produced (1) by intraperitoneal injections of iodine, (2) by laparotomy and trauma to the intestine and (3) by the production of an infective peri-

47. Guggenheim, M., and Loeffler, W.: Biochem. Ztschr. **74**:208, 1916.

48. Dale, H. H.: J. Pharmacol. & Exper. Therap. **6**:147, 1914-1915.

49. Wolf, C. G. L., and Canney, J. R. C.: Lancet **1**:707, 1926.

50. Arai, K.: Arch. f. d. ges. Physiol. **193**:359, 1922.

tonitis. Klee and Grossmann [51] reported that they had given choline intravenously in 120 cases, only a few of which, however, have been cases of ileus. They used pure choline hydrochloride, one ampule of which contained 0.6 Gm. of the drug. They added the drug to 240 cc. of sterile warm saline solution and introduced the solution into a vein slowly by gravity. Holt and Grossman [46] advocated a dose for man of 600 mg. per kilogram of body weight, given over a period of seventeen minutes; favorable case reports are included. Magnus,[45] in 1925, advised a dose of 10 mg. of choline per kilogram of body weight in man. This dose, he said, should not be given faster than 0.6 mg. per kilogram per minute; the injection of such a dose occupies seventeen minutes. Carlson, Smith and Gibbens [52] attempted to determine the action of choline on the alimentary tract of intact dogs. Using barbital anesthesia, introducing rubber balloons into various parts of the gastro-intestinal tract, thereafter closing the abdomen with as little trauma as possible, and recording movements of the intestine by means of a water manometer, they found the effect of choline on the motor phenomena variable, consisting of: (1) pure inhibition of tonus and motility, (2) inhibition of tonus and motility followed by a period of increased tone and (3) a rather exceptional observation, increased tonus and motility without inhibition. The small intestine was found to be most sensitive to the action of choline; it characteristically showed inhibition of tone and motility, followed by increased tone; sometimes pure inhibition or pure augmentation of tone was noted. The stomach was found usually to be insensitive to small doses, but when larger doses were given it usually showed late and temporary increases of tone. The transverse portion of the large intestine usually exhibited depressions of tone and motility, but occasionally showed slight increase of tone. LeHeux,[29] by means of roentgenographic studies, was able to demonstrate that the administration of choline stimulated the movements of the stomach and small intestines and hastened the passage of intestinal contents through the lumen of the large bowel. Von Kühlewein [53] found by fluoroscopic studies that chloroform anesthesia produced, within a period of two hours, an ileus that lasted for twenty minutes. This variety of ileus was relieved to a large extent by the injection of from 0.005 to 0.15 Gm. of choline hydrochloride per kilogram of body weight. Immediately after the administration of this dose of choline, definite evidences of peristalsis could be seen. Guggenheim and Loeffler [47] expressed the belief that the activating substance in intestinal movement is in reality not choline but acetyl choline. Brunner and Weigand [10] expressed the belief that acetyl choline should not be used

51. Klee, P., and Grossmann, O.: München. med. Wchnschr. **72**:251, 1925.
52. Carlson, A. J.; Smith, E. A., and Gibbens, I.: Am. J. Physiol. **81**:431, 1927.
53. von Kühlewein, M.: Arch. f. d. ges. Physiol. **191**:99, 1921.

clinically for the relief of ileus because of the danger of unfavorable associated actions of the drug.

The Action of Hypertonic Sodium Chloride Solutions.—Ross,[12] in 1926, in experimental animals, using a rubber balloon introduced into the normal intestinal canal and connected by means of rubber tubing to a manometer, showed that following the injection of a 30 per cent solution of sodium chloride in a dose from 0.33 to 0.166 Gm. per kilogram of body weight, there was an immediate increase in tone, followed by marked peristalsis. Injection of sodium chloride in this manner succeeded in producing effects in cases in which both physostigmine and pituitary extract had failed to produce any response. He reported three clinical cases in which the intravenous injection of hypertonic salt solution was successful in overcoming ileus after all other measures had failed. Coleman,[54] in 1927, working on the basis of Orr's suggestion that 3 per cent sodium chloride solution can be used in cases of ileus to combat intestinal paralysis, reported thirty-eight clinical cases occurring over a period of six years, from January, 1921, to December, 1926. The cases are divided into two groups. In the first series in which saline solution was not used, they reported twenty cases of ileus with ten deaths, a mortality of 50 per cent. In a second series of cases, numbering eighteen, making use of 3 per cent sodium chloride, they reported only two deaths, or 11.1 per cent. They admitted that the series of cases was small, but they expressed the opinion that the two series are comparable and that the decreased mortality in the second group of cases is due entirely to the use of the 3 per cent sodium chloride solution. McIntosh and Owings,[9] using a special technic for recording increases of intestinal pressure in animals, found that concentrated solutions of sodium chloride were capable of increasing the intra-intestinal pressure. Raine and Perry,[55] using rabbits and employing a special technic for the recording of intra-intestinal pressure, found that in obstructed animals the intravenous administration of 5 per cent sodium chloride stimulated peristalsis sufficiently to cause propulsion of the intestinal contents and give relief from increased intra-intestinal pressure.

REPORT OF EXPERIMENTAL RESULTS

Preliminary Note.—The experimental results to be reported are presented in as objective terms as possible. The figures for blood pressure are subsequently given and represent absolute values as recorded by the mercury manometer. Increases in intestinal tone and movement are reported also in terms of figures. These figures, how-

54. Coleman, E. P.: Anesth. & Analg. **6**:210, 1927.

55. Raine, F., and Perry, M. C.: Intestinal Obstruction, Arch. Surg. **19**:478 (Sept.) 1929.

ever, represent no absolute values, but rather millimeters of excursion of the recording point on the kymographic drum. As the excursion of such a recording lever depends not only on the amount of movement in the intestine but also on variable mechanical factors, such as the length of the lever and the distance of the fulcrum from the point of application of force, these figures are of only relative significance. However, as the physical disposition of apparatus was not changed during the entire course of the experiments reported in this communication, the figures given are directly comparable, and the amount of absolute movement of the writing point becomes of comparatively little importance.

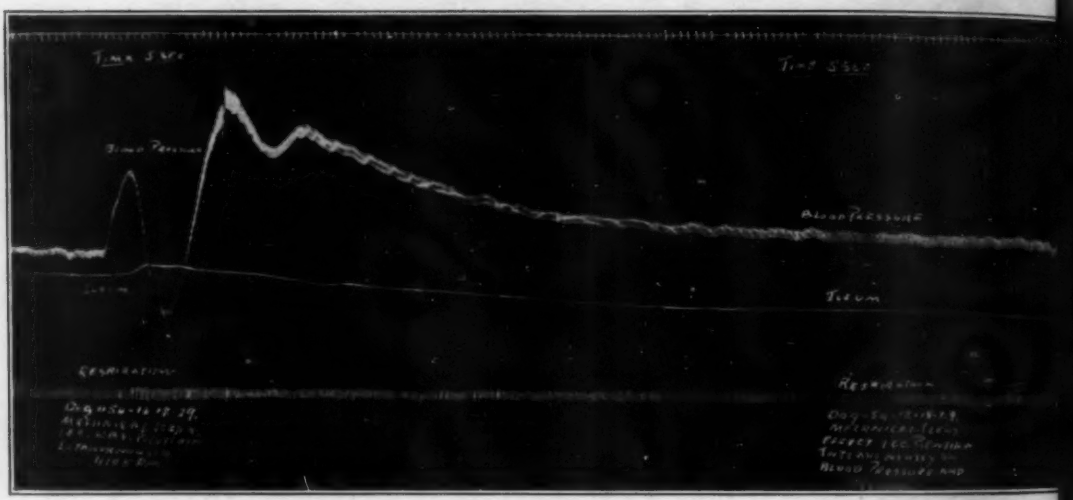

Fig. 1.—Kymographic tracing, showing the effect of the injection of 1 cc. of obstetrical pituitary extract into an animal with an artificial obstruction of forty-eighty hours' duration. The effect on the blood pressure is typical. There is an initial phase of increased blood pressure, a second phase of decreased blood pressure to a low level and a third phase of increase of blood pressure to a new high level, followed by a progressive and prolonged decrease to normal. The effect on the ileum is somewhat atypical in that a slight preliminary increase in tone is noted, but this is transient and is followed by a typical effect, namely, a progressive decrease in tone and absence of stimulation of motor activity.

The Effect of Pituitary Extract.—The effect of the intravenous or intramuscular injection of 1 cc. of pituitary extract was observed twenty-nine times in twenty-four animals. Twenty of these observations were made on normal animals and nine in animals with a forty-eight hour old mechanical obstruction.

The effect of pituitary extract in the case of normal animals was as follows:

(*a*) On the Blood Pressure: The characteristic effect of the injection of pituitary extract on the blood pressure consisted of three phases: (1) a transitory increase, which was moderate in degree, (2) a subsequent depression to a value below normal and (3) a subsequent increase soon thereafter to a level much greater than before. After this the effect tended to be persistent or to subside, the blood pressure being maintained for many minutes thereafter at a relatively high level or

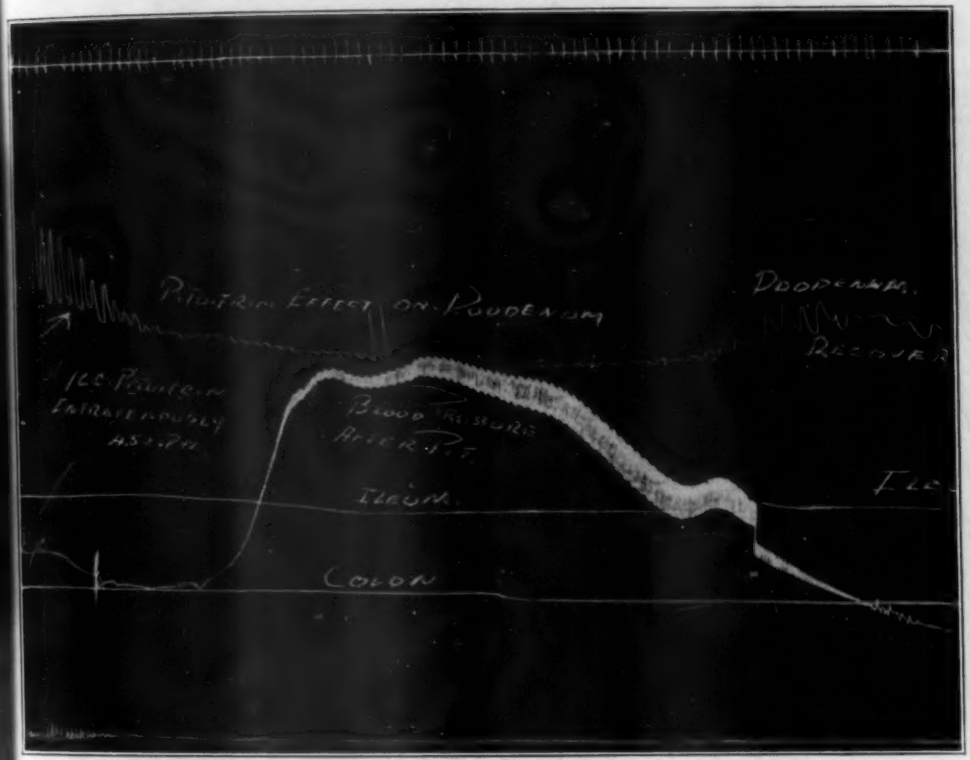

Fig. 2.—Kymographic tracing, showing the effect of the intravenous injection of 1 cc. of pituitary extract on the blood pressure, duodenum, ileum and colon. Within about a minute the blood pressure shows a marked increase which is sustained with slight variations for a period of about two minutes after which it progressively decreases during a period of about three minutes to a point below the normal level. Within a minute duodenal movement, which previous to the injection had been considerable, was reduced almost to the vanishing point, and a moderate decrease in intestinal tone occurred. In about five minutes duodenal movements began to be reestablished. The effects on the ileum and colon are slight. There is possibly a slight decrease in tone in both ileum and colon.

a gradual decrease in pressue then occurring for a similar period of time (fig. 1). Although this was the effect characteristically seen, variations were not infrequently encountered. In fact, in certain rare

cases injection of the drug produced a simple depression in the blood pressure. In seventeen of the twenty observations the first phase of initial rise in blood pressure, as previously described, was encountered. This occurred in from one to five minutes, and the average increase in blood pressure encountered was 37 mm. of mercury. In two cases during a comparable initial period there was no change in the blood pressure, and in one case a slight depression was encountered. In the succeeding period of from one to five minutes, the blood pressure showed the characteristic secondary decrease in six of the observations. The average decrease was 32.5 mm. of mercury, the initial normal blood pressure of the animal being taken as a standard. In seven

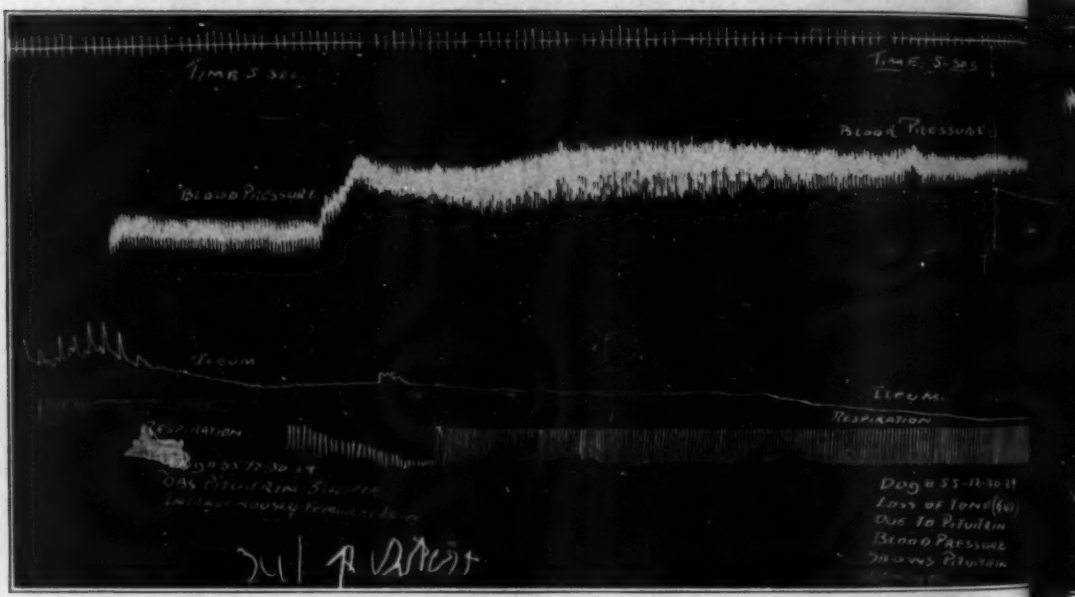

Fig. 3.—Kymographic tracing, showing the effect of 1 cc. of pituitary extract on the blood pressure and on the ileum. In this case about two minutes after the injection of pituitary extract the blood pressure increased rather abruptly and remained for at least ten minutes at a somewhat elevated level. Within one minute movement in the ileum, which previously had been considerable, ceased almost completely, and a decrease in intestinal tone occurred which persisted for at least ten minutes.

cases in the second phase the blood pressure showed no decrease, but remained sustained. In the other cases (namely, seven) variations of blood pressure during the second phase interfered with the interpretation of the results obtained. In the third phase of the reaction, four of the animals showed still further increases in the blood pressure, the average increase being 31 mm. of mercury. Animals that previously had

shown a sustained effect during the second phase continued to show this effect, and in the animals that had shown no distinct change in the second phase, no characteristic effect was seen in the third stage.

(*b*) On the Intestine: The characteristic effect of pituitary extract on the intestine was one of decrease in tone and inhibition and peristaltic movement. There were, however, a few notable exceptions to this rule. Quoting figures from the statistical study, decrease in tone was noted in sixteen of the twenty cases; no change of tone was encountered in two cases, and in two cases actual increases of tone occurred. The average decrease in tone in all cases in which the decrease

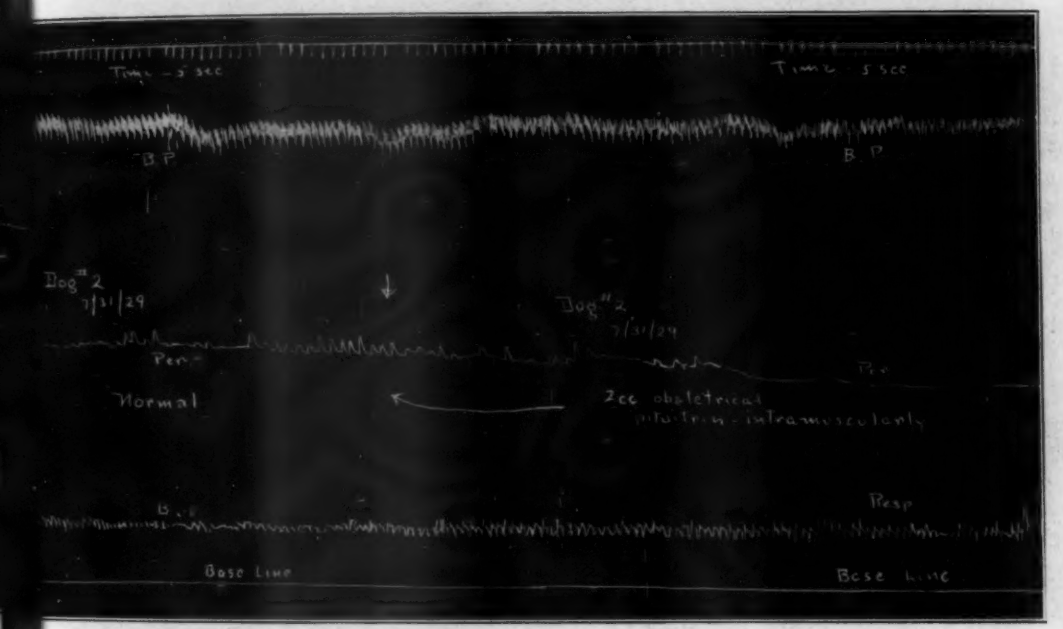

Fig. 4.—Kymographic tracing, showing the effect of the injection of 2 cc. of obstetrical pituitary extract intramuscularly. No noticeable effect on the blood pressure is seen. The effect on the ileum is characteristic. Within two and one-half minutes, intestinal movement, which previously had been rather active, subsided, and moderate decrease in intestinal tone ensued.

could be measured was 7.5 mm. In the two cases that showed increases of tone (10 per cent of the cases) the effect was pronounced, the average increase being 26 mm.

In 75 per cent of the cases (fifteen cases) the amplitude of intestinal movement either remained as before the injection (five cases, 25 per cent) or decreased somewhat. The average decrease was 3.2 mm. In 25 per cent of the cases, that is, in five cases, injection of the drug resulted in increased amplitude of intestinal movement, averaging 5 mm.

(*c*) Effect on Respiration: No constant effect was noted on the respirations of the animals used. In nine cases interpretation of the respiratory tracing was not clear. In five of the remaining cases the injection of pituitary extract produced no effect, and in five it produced a moderate decrease in respiratory excursion.

The effect of pituitary extract on animals with obstruction was as follows:

(*a*) Effect on the Blood Pressure: On the blood pressure the injection of pituitary extract invariably (except one case) produced

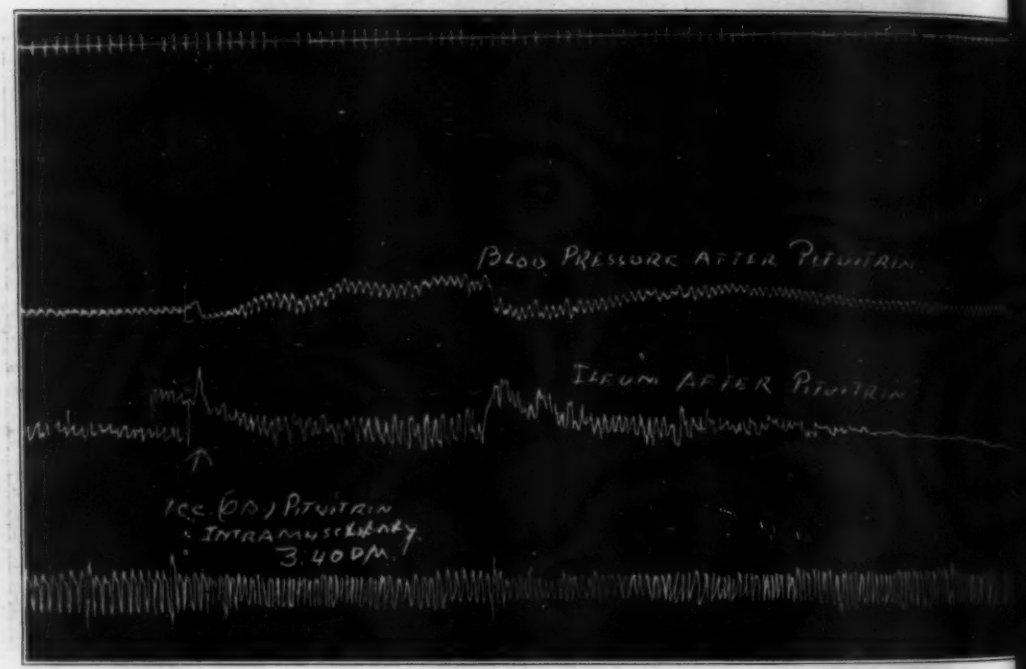

Fig. 5.—Kymographic tracing, showing the effect of the intramuscular injection of 1 cc. of obstetrical pituitary extract. In this case relatively little effect on the blood pressure is seen, although a transitory (two minutes) slight increase in the blood pressure may have been due to the effect of the drug. After five minutes, intestinal motility in the ileum, which previously had been active, subsided, and a progressive decrease in tone ensued. The latent period in this case is rather long, but the pituitary extract was injected intramuscularly, and this may account for the retardation of the effect.

an initial phase of temporary increase which occurred in from one-half to three minutes. The average increase during this phase was 41.8 mm. of mercury. In the second phase, within one-half minute or longer, the blood pressure decreased on an average of 56 mm. in five of the nine cases. A third phase occurred in four of the animals within a

minute or two, consisting of an increase of blood pressure, averaging 56.5 mm. In one of the nine animals the blood pressure showed no noticeable effect. In one case the initial rise of blood pressure was sustained at an increased level of 35 mm. of mercury. In two cases the initial rise in blood pressure was immediately followed by a progressive decrease.

(b) Effect on the Intestines: In six of the nine animals noticeable decreases in intestinal tone followed the injection of pituitary extract. In four animals the average decrease in tone was 9.2 mm. The other two animals showed unmeasured decreases. Only one animal showed

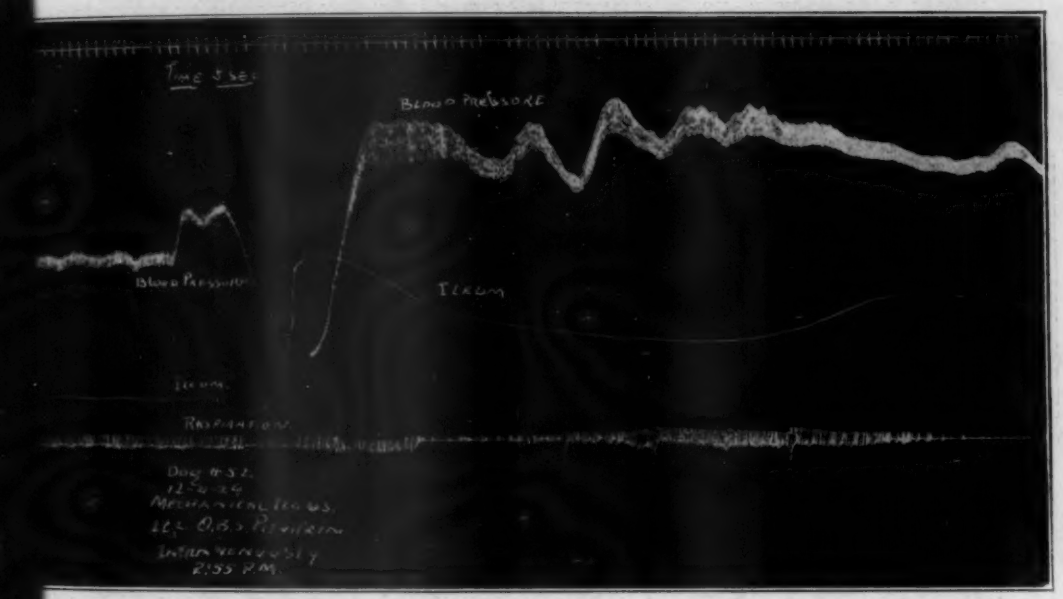

Fig. 6.—Kymographic tracing, showing the effect of the intravenous injection of 1 cc. of obstetrical pituitary extract. The effect on the blood pressure is typical, showing an initial increase, a second phase of decrease and a third phase of increase to a new high level. In this instance the high blood pressure level was maintained for a considerable period of time. The effect on the intestine was somewhat atypical, showing a preliminary decrease in tone, followed by a marked and more or less prolonged increase in tone. Complete cessation of intestinal movement was seen, although the normal movement in the ileum in this case was only slight.

an increase in tone. This was considerable (50 mm.), but was temporary, lasting only a minute. In none of the animals was the amplitude of intestinal movement increased. One animal showed a reduction in amplitude of 20.5 mm.; two animals showed a decrease which was just appreciable (1 mm.), and in the remaining animals the amplitude of movement was unaffected.

(*c*) Effect on Respiration: The effect on respiration seen in these animals was virtually nil. In three cases, however, the respiratory amplitude seemed to be somewhat decreased.

(*d*) Comparison of the Effect of Pituitary Extract in Normal Animals and in Animals with Obstructed Guts: The series of animals subjected to the injection of pituitary extract is admittedly small. The effect on the obstructed gut is similar to that on the normal gut, and any statement further than this would seem to be unjustified in the light of the relatively inconsiderable number of animals used and the considerable number of variations noted.

Exceptionally, pituitary extract seems to be capable of producing decided increases in tone in the intestinal musculature. In paralytic ileus such increases in tone, so far as we have been able to observe, are of much greater value in extruding material from the gut than increases

Fig. 7.—Kymographic tracing, showing the effect of the intravenous injection of 1/50 grain of physostigmine into a normal animal. In this tracing duodenal, ileal and colonic tracings were recorded simultaneously. The effect on the blood pressure is typical, showing a considerable, slow increase in blood pressure followed by a prolonged and progressive decrease. The effect on the duodenum is a very decided and prolonged increase in the amplitude of intestinal movement, accompanied by a slight increase in tone. The effect on the ileum is typical—a slow progressive increase in tone with the ultimate production of a rather marked increase in the amplitude of intestinal movement. The effect on the colon is one of increased movement, but the tone itself remains relatively unchanged.

in intestinal motility. The reason for this is fairly obvious. The contents of the gut characteristically consist of fluid material and gas. Intestinal movements alone may merely mix such contents without propelling them, peristaltic waves passing the length of the gut, but the contained fluid and gas regurgitating through the advancing ring of peristaltic constriction as soon as any considerable increase in intraintestinal pressure is produced ahead of the peristaltic wave. If pituitary extract would always increase intestinal tone, as it does in the exceptional case, it would be of considerable value. Apparently, those who

have reported favorably on the clinical use of pituitary extract have been fortunate enough to encounter the exceptional action of the drug.

The Effect of Physostigmine.—Physostigmine in the form of physostigmine sulphate was injected twenty-four times into twenty-one dogs. The dose of the drug was 1/50 grain (0.0013 Gm.) injected intravenously. Ten of the observations were on animals that had undergone experimental mechanical obstruction forty-eight hours previously. The other fifteen observations were on normal animals.

The effect of physostigmine on normal animals was as follows:

(*a*) The Effect on Blood Pressure: In every case, except one, the blood pressure increased, following the injection of physostigmine. The amount in every case was significant. The single case in which no increase was noted showed a decrease of 20 mm. of mercury. Earlier

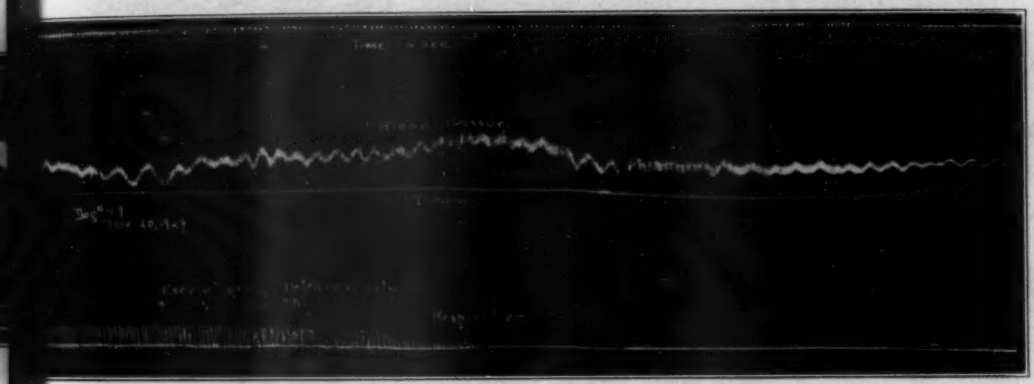

Fig. 8.—Kymographic tracing showing the effect of the injection of 1/50 grain of physostigmine intravenously into a normal dog. The effect on the blood pressure is typical and consists of an irregular, gradual increase in blood pressure. The effect on the ileum in this case is virtually nil. However, on close inspection, variations in tone can be appreciated.

in the afternoon in which the experiment was performed, this animal had received a prior injection of the same drug. The average increase in blood pressure shown by the other animals was 17.2 mm. The average duration of the rise of blood pressure caused by the injection was three and eight-tenths minutes. In all cases the blood pressure returned either to a normal or to a subnormal level, and the average duration of the decrease to a normal level was twelve and seven-tenths minutes. In two of the seventeen cases the blood pressure eventually fell to a level of 20 mm. below that seen at the time of injection.

(*b*) Effect on the Intestines: With the exception of one instance, the tone of the intestine invariably rose as the result of the injection of physostigmine. In the atypical case there was a decrease of 10 mm. in tone which lasted for twenty minutes. The average increase in

tone in the fourteen cases in which this effect was seen was 26 mm., and the average latent period between the time of injection and the beginning of the effect on tonus was four minutes. The injection of physostigmine characteristically produced augmentation of the intestinal movement. The average increase in amplitude of these movements was 3.9 mm., and "tonus waves" were apparently produced by the drug in two instances. Atypical effects on intestinal movement were seen in two instances. In these two cases there was no increase in movement. The drug simply showed failure to produce a typical augmentation.

(*c*) Effect on Respiration: The effect on respiration was inconstant. The amplitude of respiration was apparently decreased in four cases, increased in one case and showed no effect in the others.

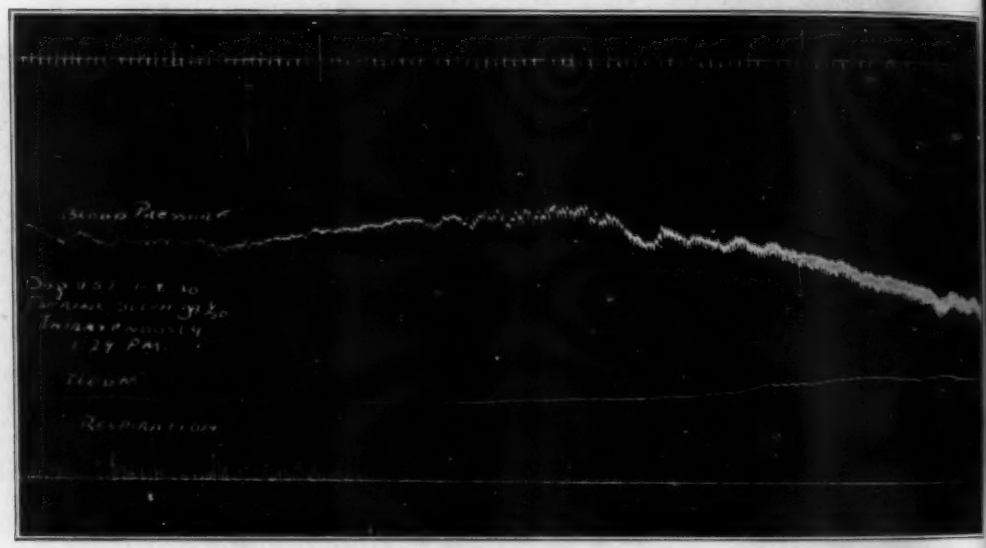

Fig. 9.—Kymographic tracing, showing the effect of the injection of 1/50 grain of physostigmine sulphate intravenously into a normal dog. The initial effect on the blood pressure is typical, showing a moderate increase. The progressive decrease, however, which characteristically follows, is exaggerated in this case, and the blood pressure actually decreases to a new low level. The effect on the ileum is typical in that the tone shows a gradual increase, and definite, though slight, intestinal movement is initiated.

The effect of physostigmine on animals with obstructed guts was as follows:

(*a*) Effect on Blood Pressure: In all but two cases the effect of the injection of physostigmine was to increase the blood pressure. The average increase in the thirteen cases showing this typical effect was 32 mm. of mercury; the average latent period between the injection of the drug and the beginning of effect on blood pressure was four and three-tenths minutes. The other two cases showed an insignificant

decrease in blood pressure, the average being 3 mm. The average latent period of this reaction was six minutes.

(*b*) Effect on the Intestine: The characteristic effect of physostigmine was to increase both the tone of the intestine and the amplitude of its contractions.

(*c*) Effect on Tone: In eight cases there was an average increase in tone of 10.7 mm., but in one case the tone subsequently fell to a subnormal level. The average latent period between the injection of the drug and the beginning of the effect on tone was nine and two-tenths minutes. In three cases the tone of the intestine was unaffected; in four cases the tone actually fell, but the average decrease in these four cases was only 4 mm.; the decrease in tone in the latter cases, being only relatively slight and being gradual, could not be determined with

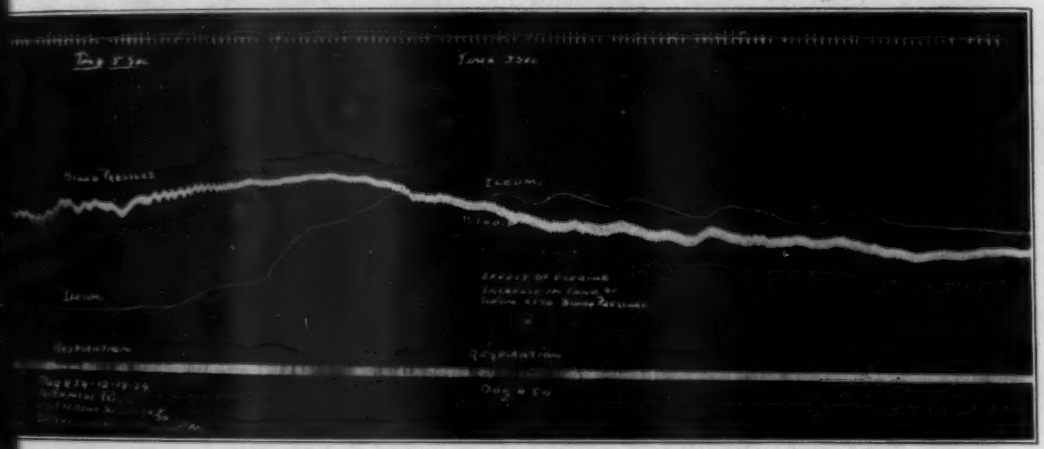

Fig. 10.—Kymographic tracing, showing the effect of the injection of 1/50 grain of physostigmine sulphate intravenously into a dog with mechanical ileus. The effect on the blood pressure is characteristic. A gradual initial rise in blood pressure was followed by a progressive decrease to a normal or even a subnormal level. The effect on the ileum is characteristic, but shows a rather exaggerated increase in tone and the ultimate development of tonus waves, superimposed on which is evidence of slight intestinal movement.

accuracy. The effect of physostigmine on intestinal motility was not constant, but was decidedly in the direction of increased movement. A definite increase was noted in seven cases, the average increase in amplitude being 3.8 mm. In six cases intestinal movement was unaffected. In two cases the movement of the intestine was decreased, the average amount being 3 mm.

(*d*) Effect on Respiration: The effect of physostigmine on respiration was found to be negligible.

(*e*) Comparison of the Effect of Physostigmine in Normal Animals and in Animals with Obstruction: A consideration of the figures pre-

sented would seem to indicate that the effect of physostigmine on the animal with an obstructed gut is more consistent and profound than the effect on normal animals. Increases in intestinal tone were noted in only slightly more than one half of the normal animals, whereas 90 per cent of those with obstruction showed this effect. A similar effect was noted on the amplitude of intestinal movement, whereas the amplitude was increased in less than half the normal cases; 80 per cent of the cases that had undergone previous intestinal obstruction showed definite augmentation. The effect on blood pressure in the two series was reversed in that injection of physostigmine produced an average increase in blood pressure nearly twice as great in normal animals as in those with obstruction.

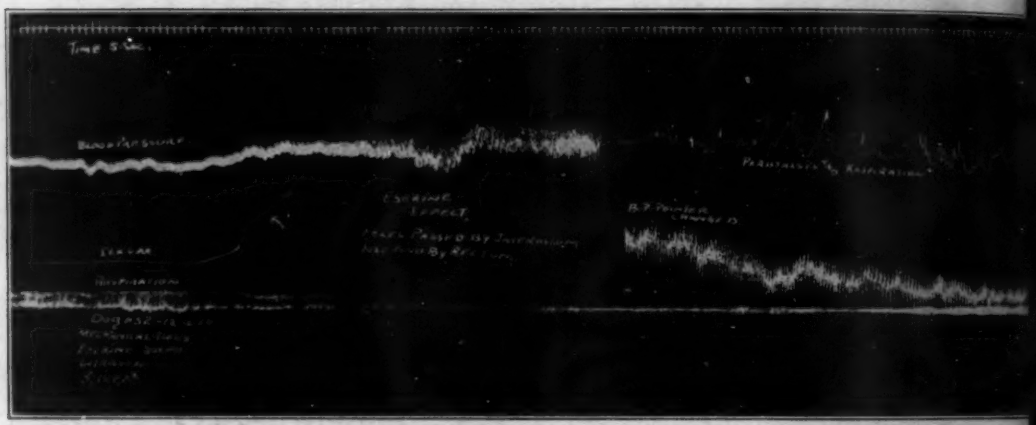

Fig. 11.—Kymographic tracing, showing the effect of the intravenous injection of 1/50 grain of physostigmine sulphate into a dog in which artificial mechanical ileus had been produced forty-eight hours previously. The effect on the blood pressure is somewhat atypical in that no significant increase in blood pressure is evident. The interruption in the blood pressure tracing, which occurs about the middle of the graph, is not significant, since a mechanical readjustment of the writing point was made at this time. The effect on the ileum is typical but greater than that ordinarily seen. There is a rather sharp, progressive increase in tone followed by a decided increase in the amplitude of intestinal movement. Toward the end of the tracing certain of the irregularities which can be seen probably represent respiratory components, pressure changes being transmitted from the diaphragm to the intestine. The writing point of the blood pressure apparatus was depressed in order to make this part of the tracing visible.

The Effect of Choline.—Choline was administered four times to four normal animals. A pure preparation of choline hydrochloride was used, and this was dissolved in 100 cc. of physiologic solution of sodium chloride. The solution containing the drug was injected into the vein of the animal by gravity, and it was allowed to run only very slowly.

(*a*) Effect on Blood Pressure: In three of the four animals the injection of choline was followed by rather rapid decreases in the blood pressure. Since the decreases in the blood pressure were directly proportionate to the rapidity with which the solution was introduced, the amount of blood pressure decrease is of little significance. The average was 13.3 mm. In one animal the blood pressure showed an increase of 10 mm. This increase in blood pressure was attributed not to the drug itself, but rather to the effect of the sodium chloride solution which

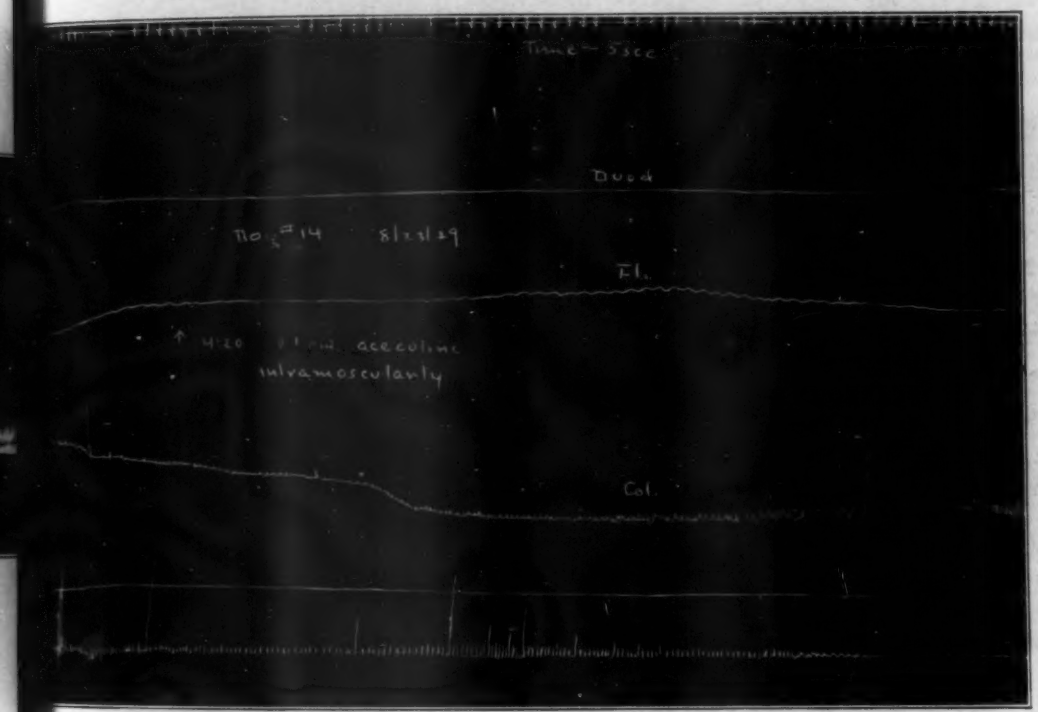

Fig. 12.—Kymographic tracing, showing the effect of the intramuscular injection of 0.1 Gm. of acetyl choline into a normal dog. The effect shown on the blood pressure is typical, manifesting a gradual decrease to a low level, which is subsequently maintained. Duodenal, ileal and colonic tracings are recorded. Little or no effect is noted on the duodenum. In the ileum, a slight increase in tone and a slight increase in amplitude of movement is recorded. In the colon, no change of either tone or amplitude is seen.

temporarily increased the blood volume. This view seems to be corroborated by the fact that two of the three animals that showed initial depressions of the blood pressure showed subsequent increase, one to a level of 30 mm. and the other to a level of 60 mm. above normal.

(*b*) Effect on Intestinal Tone and Motility: The effect of this drug on intestinal tone and motility was inconstant and insignificant. In only

one of the four animals was an increase in the tone noted, and this was relatively slight, 8 mm. The effect on the amplitude of intestinal movement was inconstant. One animal showed no effect; another animal showed an insignificant increase (1 mm.), and the remaining two animals showed insignificant decreases in the amplitude of movement.

Effect of Acetyl Choline.—Acetyl choline was injected subcutaneously ten times into as many normal animals.

(*a*) Effect on the Blood Pressure: The invariable effect of acetyl choline on the blood pressure was a decrease which occurred either immediately or within a period of five minutes. The decrease averaged 66.6 mm. of mercury, which is a considerable depression. In all but

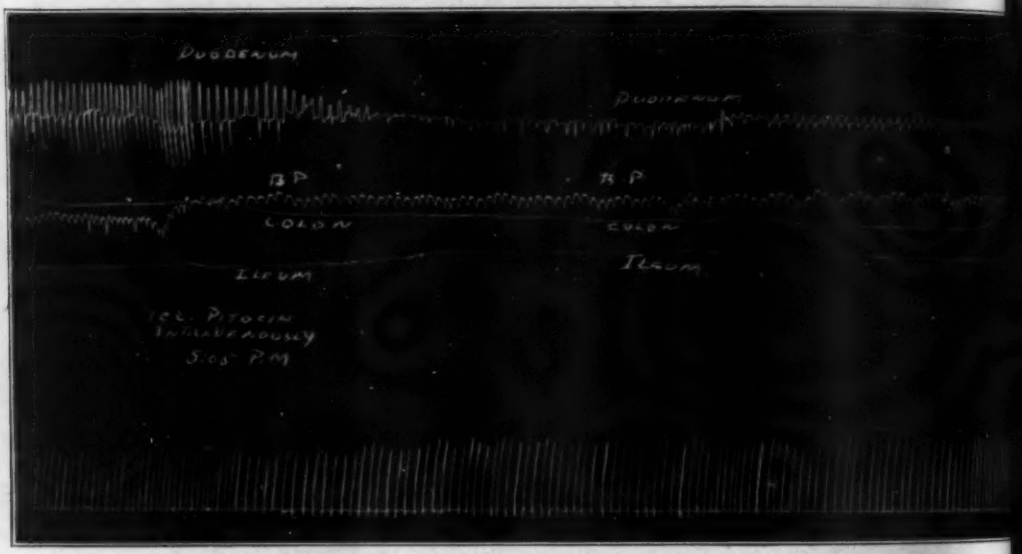

Fig. 13.—Kymographic tracing, showing the effect of the intravenous injection of 1 cc. of pitocin into a normal dog. The blood pressure is relatively unaffected, but possibly slightly increased. The effect on the duodenum in this particular case was a diminution in the amplitude of duodenal movements. In the colon there was relatively little effect, except possibly a slight decrease in tone. In the ileum there was possibly a slight increase in tone and possibly also some increase in intestinal movement.

three of the cases the blood pressure remained subsequently at a relatively constant low level. In two of the remaining cases the blood pressure increased gradually, but never attained a normal level. In only one case did the blood pressure subsequently surpass the normal value.

(*b*) Effect on the Intestines: The effect on the intestinal tone was variable. In four cases, 40 per cent, there was an increase, averaging 21 mm. In five cases decreases were seen, averaging 6 mm., and in one case no change was noted. The effect on the amplitude was also

variable, but was generally in the direction of increases. In six cases the increase of amplitude averaged 4.3 mm. Three cases showed decreases in amplitude, averaging 2 mm., and in one case there was no apparent effect on the animal.

The Effect of Pitocin.—One cubic centimeter of pitocin was injected intravenously into each of five normal animals.

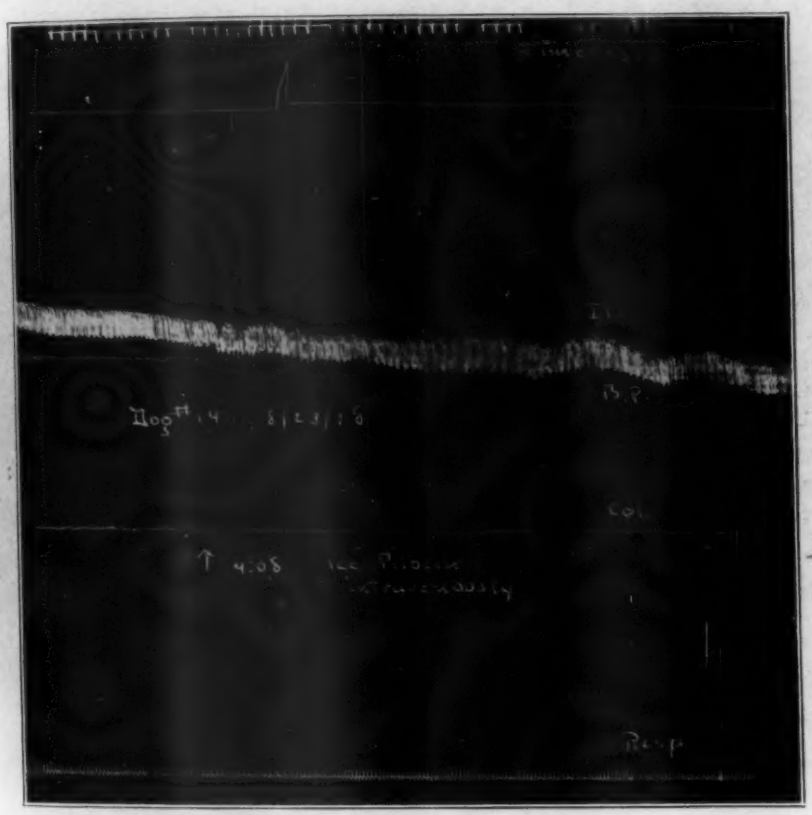

Fig. 14.—Kymographic tracing, showing the effect of the intravenous injection of 1 cc. of pitocin into a normal dog. The only effect seen in this tracing is on the blood pressure, and in this case there was a progressive decrease. No effect on either tone or amplitude of intestinal movement was seen in the duodenum, ileum or colon.

(*a*) Effect on Blood Pressure: No conclusions can be drawn as to the effect of pitocin on the blood pressure, since in two cases no effect was recorded; in two cases increases of 6 and 10 mm. of mercury, respectively, were found, but one of these cases, the latter, showed a subsequent decrease of blood pressure to 50 mm. below normal, the

latter low level being sustained. In the other animal there was a progressive, slow decrease in blood pressure of 30 mm.

(*b*) Effect on the Intestines: No constant effect on the intestine was noted when pitocin was used. In all cases in which this particular drug was administered simultaneous tracings of the ileum, duodenum and colon were recorded. As to the effect on tone, in no case was an increase noted in the ileum. In one instance the tone of the duodenum was increased, and in another it was decreased, whereas in two cases the

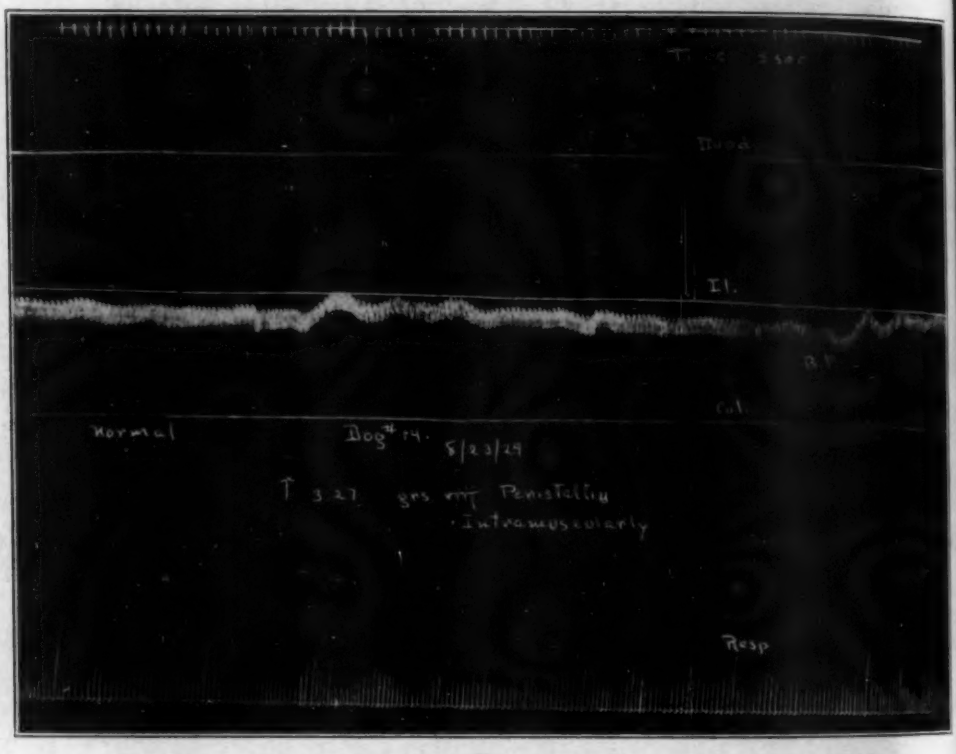

Fig. 15.—Kymographic tracing, showing the effect of the intramuscular injection of 8 grains of peristaltin into a normal dog. The tracing is typical in that no significant effect is noted in the blood pressure or in the tone or amplitude of intestinal movement in the duodenum, ileum or colon.

tone of the colon was definitely decreased. The effect of this drug on the amplitude of intestinal movement was variable; sometimes slight increases were noted and at other times slight decreases.

(*c*) Effect on Respiration: Pitocin showed no appreciable effect on the respiration.

Effect of Peristaltin.—The effect of peristaltin was recorded fifteen times in twelve animals. It was employed in five instances on four animals with obstruction and ten times in eight normal animals.

The effect of peristaltin on normal animals was as follows:

(*a*) Effect on Blood Pressure: Peristaltin showed no constant reaction on the blood pressure of normal animals. There was a decrease in blood pressure in five cases, averaging 12 mm. In two cases there was an increase in blood pressure of 10 mm. each. In the remaining cases no change was evident.

(*b*) Effect on Intestinal Movement: The effect of peristaltin on intestinal movement was either nil (four cases) or in the direction of decreases (six cases) with an average of 8.3 mm. The effect on the amplitude of intestinal movement was usually negligible. It was nil in four cases. Decrease in amplitude occurred in five cases, the average being 1.1 mm., and there was an insignificant increase of amplitude in one case (1 mm.).

Fig. 16.—Kymographic tracing, showing the effect of the intravenous injection of 20 per cent sodium chloride solution. No significant effect is noted on the blood pressure. The ileum shows a slight increase in tone, lasting four minutes. At the end of this period, intestinal movement is increased slightly. The respirations show an increase in rate and amplitude.

(*c*) Effect on Respiration: In thirteen of the eighteen cases no respiratory changes were noted, and in the other two cases the effect was questionable.

The effect of peristaltin on animals with obstructed guts was as follows:

(*a*) Effect on Blood Pressure: In the five cases in which peristaltin was used three of the animals showed decreases in blood pressure, averaging 20 mm. In two of the animals no change was noted. In the two cases which showed decreases in blood pressure, the low blood pressure level was maintained.

(*b*) Effect on Intestines: The effect on the intestine was inconstant, with respect to both tone and amplitude of movement. Three cases

showed increases of tone, averaging 10.2 mm. One case showed no effect on tone, and the remaining animal showed a very distinct decrease to 65 mm. below normal. The effect on the amplitude of intestinal movement was of no significance except in one case. In this case, an increase of amplitude of 4 mm. was demonstrated.

(*c*) Effect on Respiration: The effect of peristaltin on the respiration was negligible.

The Effect of Sodium Chloride.—Sodium chloride in 20 per cent solution was injected intravenously into four animals; two of these were normal dogs, and in two of them the gut had been obstructed for forty-eight hours.

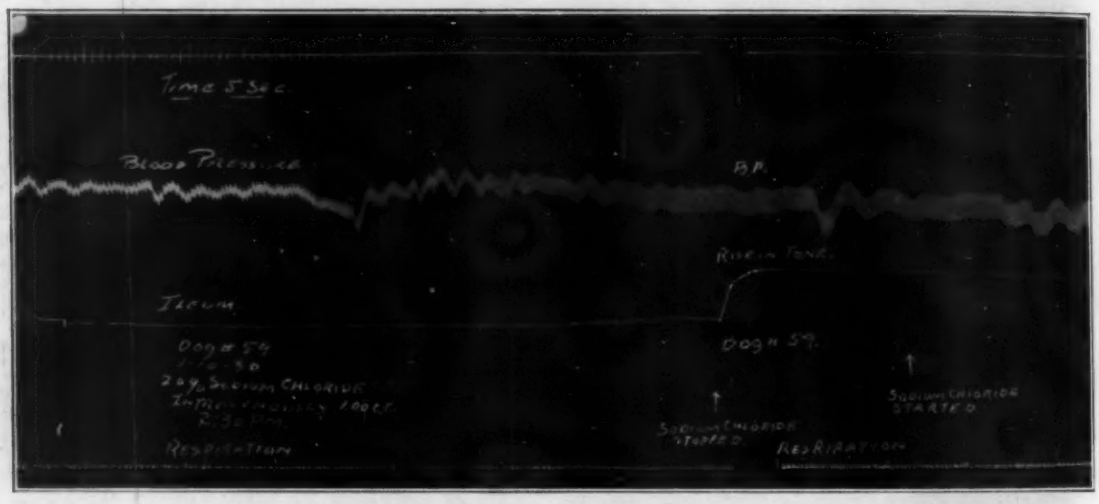

Fig. 17.—Kymographic tracing, showing the effect of the intravenous administration of 20 per cent sodium chloride solution. The blood pressure is irregular and shows a slight tendency toward progressive decrease. After a later period of about eight minutes, the ileum undergoes a rapid increase in tone, which is fairly well sustained subsequently. Very slight intestinal movement is initiated. The effect on respiration is an increase in rate without apparent increase in amplitude.

The effect of sodium chloride on normal animals was as follows:

(*a*) Effect on the Blood Pressure: The effect on the blood pressure was variable. In one animal slight variations in blood pressure were noted, but no significant increase or decrease eventuated. In the second animal the blood pressure decreased 20 mm. within a period of two minutes. This depression of blood pressure was sustained.

(*b*) Effect on the Intestine: In the first animal a progressive increase in tone of 14 mm. was noted, which attained its maximum at

the end of five minutes. In the second animal no increase in tone was noted. The effect on intestinal movement was slight, but both animals showed very feeble intestinal movement at the end of a ten minute period.

The effect of sodium chloride on animals with obstruction was as follows:

(*a*) Effect on the Blood Pressure: The effect on the blood pressure was variable. In one animal the blood pressure increased with variations over a period of eleven minutes and attained an elevation of 20 mm. of mercury. In the other animal a decrease in blood pressure of 40 mm. occurred within one-half minute. The blood pressure did not remain depressed to this low level, however, but subsequently increased 20 mm. during the course of the next three minutes.

(*b*) Effect on the Intestines: In both animals a gradual, progressive increase in tone was observed. This amounted to 48 mm. in the first animal, and reached a maximum within a period of thirteen minutes. In the second animal the maximal increase was 6 mm., attained at the end of five minutes. In both animals increases in motility were noted. The increase in amplitude of intestinal movement of the first animal amounted to 5 mm. and in the second animal to 2 mm.

COMMENT AND CONCLUSIONS

In view of the relatively large number of clinical and experimental observations that have been made on the effect of drugs on intestinal motility, it would have seemed reasonable to suppose that much more significant changes could be achieved by drug therapy than we have been able to observe. Of more than passing significance would seem to be the inefficiency of pituitary extract as an intestinal stimulant.

Careful examination of the literature with respect to the action of pituitary extract discloses two interesting facts: (1) Most of the favorable reports that have been made on this action of pituitary extract have had their basis in clinical observations, and (2) such experimental investigations as have been made under carefully controlled conditions show a relatively equally divided difference of opinion; virtually as many authorities expressed the conviction that pituitary extract depresses the tone and motility as expressed the opposite and more generally accepted view. Clinicians labor under a severe handicap in the evaluation of the action of drugs, since the psychic reactions of the clinical observer are apt to warp his judgment. There is a real tendency for clinical exaggeration of the beneficient clinical effects and a tendency to underestimate the number and degree of clinical failures.

Our results would appear to be in line with those obtained by the more careful and unprejudiced experimental investigators who have

previously published reports on the action of pituitary extract. Pituitary extract would not only seem to be an ineffective drug in the treatment for intestinal atony, but also would appear to be a dangerous drug in such a condition. Although it sometimes seems to increase the tone and motility of the intestinal musculature, the more characteristic effect is one of decrease in tone and motility. The occasional beneficial effect that might result from injection of the drug in certain cases would seem to be far outweighed by the depressant effect, which is apparently more frequently seen and is comparatively more profound. The variable effect of pituitary extract on the blood pressure is probably not sufficiently appreciated; although in most cases dependence can be placed on pituitary extract to raise the blood pressure, there are apparently cases in which actual depressions occur.

The effect of physostigmine on the intestinal tone and motility, according to our investigations, is virtually that which might be expected from a consideration of previous reports, both clinical and experimental. Although it is true that physostigmine seems never to produce significant decreases in tone and motility and therefore could scarcely be considered a dangerous drug, the stimulating effect of physostigmine would not seem to be particularly significant. The fact that this drug is perhaps the oldest substance that has been used for the purpose of stimulating intestinal motility suggests that physostigmine perhaps has some definite place in the therapeusis of intestinal atony. This is the only drug that we have found to be of consistent efficacy, and possibly the fact should be stressed that the action of this drug seems to be enhanced in intestinal obstruction, at least in intestinal obstruction no further advanced than that used for the purposes of the present experimental investigation. This presents rather interesting evidence that possibly the obstructed intestine, in the initial stages at least, is hyperexcitable; if this is correct, the value of the various other drugs used in this series of experiments would seem to be proportionately minimized. If these drugs are of no value in the stimulation of intestinal movement in a hyperexcitable intestine, they should certainly prove of no value in stimulation of the normal intestine or in an intestine in which for one reason or another the excitability is decreased.

Choline, acetyl choline, pitocin and peristaltin have proved disappointing in the present series of investigations. Apparently little dependence can be placed on these therapeutic agencies in the stimulation of either normal or hyperexcitable intestinal musculature. All in all, it would seem that the drug therapy for intestinal atony rests on a rather precarious foundation, and although the results of the present experimental investigations are by no means conclusive, they suggest a well nigh complete revision of our evaluation of the efficacy of drug therapy in the relief of conditions of intestinal quiescence.

COMPLETE OCCLUSION OF THE SUPERIOR VENA CAVA BY PRIMARY CARCINOMA OF THE LUNG*

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SAN FRANCISCO

Partial obstruction of the superior vena cava is not uncommon. On the other hand, complete obliteration either by compression or by thrombosis is unusual, and obliteration due to carcinoma is extremely rare.[1] I shall therefore in this communication note the instances reported in the literature, describe this condition and add thereto a case observed in Mount Zion Hospital.

CASES RECORDED IN THE LITERATURE

The first case of obstruction of the superior vena cava was noted in 1806, by Corvisart. At intervals since then cases have been reported and collected as follows: Oulmont,[2] 1856; Fischer,[3] 1904; Rauth,[4] 1911, and Dana,[5] 1922. Dana, after a critical review of all previously tabulated cases, accepted reports of interference with the circulation in the superior vena cava by "primary carcinoma" of the lung in twenty-three instances, only six of which were verified as carcinoma, and by carcinoma primary in the bronchi in fourteen observations. To these must be added Dana's own proved case, bringing the total to thirty-eight. My search of the literature fails to reveal any further reported cases.

Approximately one half of the cases of complete obstruction of the superior vena cava by primary carcinoma of the lung or bronchus showed invasion of the walls of the cava. In the remaining half, the obstruction was due to compression by the tumor mass with or without thrombosis of the cava. The case to be reported in this paper is one of primary peribronchial carcinoma, with complete obstruction of the superior vena cava by compression plus thrombosis.

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* From the Thoracic Surgery Clinics of Mount Zion Hospital and the University of California Medical School.

1. Osler, William: On Obliteration of the Superior Vena Cava, Bull. Johns Hopkins Hosp. **14**:169 (July) 1903.

2. Oulmont: Soc. méd. d'observation **3**:463, 1856.

3. Fischer: Inaug. Diss., Halle, 1904.

4. Rauth: Inaug. Diss., Univ. zu Giessen, Borna-Leipzig, Robert Noske, 1911.

5. Dana, H. W., and McIntosh, R.: Obstruction of the Superior Vena Cava by Primary Carcinoma of the Lung, Am. J. M. Sc. **163**:411 (March) 1922.

ETIOLOGY

Occlusion of the superior vena cava by either compression or thrombosis may be brought about by any one of several factors. Aneurysm of the aorta and mediastinal tumors have been found to be responsible for the condition in about 55 per cent of the 300 odd cases reported in the literature, each in approximately the same frequency. Carcinoma of the lung, bronchi and adjacent organs produced the obstruction in about 25 per cent more of the instances. The remaining 20 per cent are ascribed to various diverse factors relatively infrequently observed. In this group have been noted such causes as: mediastinitis, periaortitis, contraction of scar tissue, especially tuberculous or syphilitic, compression by mediastinal tumors other than carcinoma, ecchinococcus cysts, struma, transportation of carcinomatous masses from distant organs, sclerosis of the bronchial glands, phlebitis and thrombophlebitis.

Whereas aneurysm is doubtless becoming more infrequent because of modern antisyphilitic therapy, carcinoma appears to be on the increase. Likewise, inflammatory lesions as a factor in producing the obstruction of the cava appear with greater regularity in the more recent reports. Inflammatory lesions extending into the mediastinum cause traction and pressure on the adjacent organs (i. e., vena cava superior) through induration of the connective tissue. This formation of firm, indurated new growth of connective tissue in the mediastinum has been termed indurative (or adhesive) mediastinopericarditis. Clinically, this condition is characterized by pulsus paradoxus and turgescence of the jugular veins. The commonest cause is inflammation of the bronchial glands, which may be due to syphilis or tuberculosis. Severe rheumatic pericarditis sometimes produces an inflammatory reaction that may extend to the surrounding fibrous tissue, such as the pleura, and along the large vessels.[6]

Thus, when one is confronted with a patient whose symptoms suggest compression or occlusion of the superior vena cava, intrathoracic cancer should first be considered, then "adhesive mediastinopericarditis" and its causes and finally the other varied etiologic factors that have been enumerated.

SIGNS, SYMPTOMS AND PROGNOSIS

The physical signs and symptoms of occlusion of the superior vena cava are variably striking, depending on the rapidity with which the occlusion takes place and the degree to which compensatory circulation has been established. Obliteration thereof may exist for many years with good health and a completely effected collateral circulation. Objectively, one may note cyanosis or lividity of the face; suffusion of

6. Pawel, I.: Ein Fall von Verschluss der Vena Cava Superior, Inaug. Diss., Leipzig, 1910.

the conjunctivae; prominence and staring of the eyes; edematous swelling of the neck, arms and thorax, with more or less marked dilatation of the superficial veins of the thorax and upper part of the abdomen; edema and cyanosis of the mucous membranes of the tongue, mouth, pharynx and larynx.[7] Subjectively, this venous engorgement may produce headache, vertigo, deafness, epistaxis, tinnitus, visual disturbance and somnolence or temporary loss of consciousness.[8]

The prognosis depends primarily on two factors: (1) the rapidity of development of the occlusion, or the time allowed for the development of a compensatory circulation, and (2) the prognosis in the disease entity that is the primary cause of the obstruction or thrombosis of the cava.

REPORT OF A CASE

History.—I. A., a man, aged 65, was referred by Dr. L. I. Grodsky, on May 1, 1929, with a chief complaint of swelling of the face and neck. Until one month before admission, the patient had considered himself to be in good health. Since then he had noted a fluctuating swelling of the face and neck, worse on getting up in the morning, somewhat decreased by night, but on the whole gradually increasing in severity. There was no difficulty in respiration or deglutition. There was no cough or sputum or history of recent infection of the mouth or respiratory system. There had not been noted any loss either of weight or strength. His occupation was carpet laying, but he had been unable to secure work for the past two months.

The patient was born in San Francisco and had lived there his entire life. His general health had always been good. He said that he had rarely had any illnesses, except a mild cold, one per year. He had not had diphtheria, influenza, whooping cough, asthma, bronchitis, pneumonia or tonsillitis.

About two years before, he had had an appendectomy for acute appendicitis and a hemorrhoidectomy. He had had no headaches and no trauma. His vision had been good, and the eyes were free from inflammation and pain. He had had no loss of hearing, and no pain in the ears or discharge. He had had no colds in the head, discharge, epistaxis or symptoms of obstruction. He had not consulted a dentist for ten years. He said that he had not had tonsillitis, sore throat, sore mouth or hoarseness, and no pain in the chest, cough, sputum, dyspnea, orthopnea, palpitation, night sweats or hemoptysis. His appetite had been good. The bowels had been regulated with an occasional cathartic, but there had been no gastric distress, nausea or vomiting. He had never been jaundiced. He had never had bloody, tarry or clay-colored stools. His hemorrhoids, external, had been relieved by operation two years before. There had been no dysuria, hematuria, frequency or incontinence. There had been nocturia from one to two times a night for the past six years. He said that he had not had venereal disease or any symptoms of it. He had not experienced vertigo, fainting, paralysis or muscle pains. His weight had been constant at about 165 pounds (74.8 Kg.) for the past ten years.

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7. Lamb, A. R.: Nelson's Loose-Leaf Living Medicine, New York, Thomas Nelson & Sons, 1927, vol. 4, p. 585.

8. Lilienthal: Thoracic Surgery, Philadelphia, W. B. Saunders Company, 1925, vol. 1, p. 260; footnote 6.

With the exception that one sister had died of cancer of the breast, the family history was essentially negative.

Physical Examination.—The patient was well developed, well nourished and slightly obese, about 65 years of age, sat up in bed, was not in acute distress, cooperated fairly well, was mentally clear and moved about with no apparent difficulty. The voice was rather hoarse, but was said not to have changed for several years.

The skull was symmetrical, with no exostosis, irregularities or tenderness. The scalp was clean, with no scars. The hair was normal in texture and distribution. There was generalized alopecia of the scalp. The face was round, flushed and edematous, especially at the angles of the jaw and in both parotid regions. The skin of the face and tissues above the clavicles and the sternum showed flushing, gradually fading over the shoulders. It was normal in texture, moisture and

Fig. 1.—Discoloration of the face and neck due to venous congestion, prominence of the external jugular veins especially on the left and swelling of the face and neck.

pigmentation. The eyes revealed beginning arcus senilis. They reacted to light and distance. The vision was good. The fundi showed moderate bilateral choked disks and marked distention of the retinal veins. There was right internal strabismus. The hearing was good. There was no discharge or tophi. The nose showed no deformity, obstruction or discharge. The lips revealed moderate cyanosis, and no ulcerations or fissures. The gums showed slight pyorrhea and no lead line. The tongue protruded in the midline, without tremor. The tonsils were small, without exudate or inflammation. The floor of the mouth and the upper part of the pharynx appeared edematous, but not inflamed. The results of laryngoscopic examination were negative.

The entire neck was enlarged, apparently by an edematous infiltration, to at least twice its normal size. The thyroid gland was not palpably enlarged. The veins of the neck were markedly distended on both sides. There was no bruit, stiffness, thrill or abnormal pulsations and no tracheal tug. The lymph nodes

were not enlarged. Over the left clavicle was a small wound where two days before an unsuccessful attempt had been made to remove a node for microscopic examination.

The thorax was symmetrical and moderately barrel-shaped; the expansion was fair and equal on both sides. The respirations were 24 and regular. There was no abnormal pulsation. The venules of the lower half of the anterior wall of the chest were markedly prominent. The breasts were normal.

The action of the heart was regular, the sounds clear, with no murmurs. The right border was 2 cm. from the sternum; the left, 9 cm.; the apical impulse was seen and felt in the nipple line, fifth space, 8 cm. to the left of the midsternal line. The rate was 90 per minute.

The aorta revealed no palpable or audible abnormality. Extending downward 7 cm. from the clavicle on the right and 3 cm. to the right of the sternum was an area of increased dulness. A corresponding area of dulness, most marked on the right, was made out posteriorly between the scapulae. The arteries showed radial pulses equal and synchronous, 90 per minute and of good quality. The radial and brachial arteries were moderately sclerosed. The jugular, axillary and brachial veins were markedly enlarged, tortuous and engorged. The blood pressure in the right arm was 115 systolic and 70 diastolic; that in the left arm was 120 systolic and 75 diastolic.

The lungs showed paravertebral and parasternal dulness, as noted. A few scattered moist râles were heard throughout the chest. Tactile fremitus was normal.

The abdomen was soft, lax and tympanitic throughout. No spasm, mass or tenderness was present. There was no free fluid. An egg-sized indirect inguinal hernia on the left was readily reducible. The gallbladder, spleen and kidneys were not felt. The liver showed percussion dulness from the fourth rib. The edge was smooth, and on deep inspiration was felt 1 cm. below the costal margin.

Several pea-sized to walnut-sized masses were felt in both axillae, the largest on the left; apparently these were enlarged lymph nodes. Other lymph nodes were not remarkable.

There was moderate fixation of the dorsolumbar spine.

The extremities showed no involuntary movements, tremor or wasting. There was marked clubbing of all the fingers. No changes in the joints were made out. No varicosities, scars or ulcers were present on the legs. There was no edema of the ankles. The knee jerks were active and equal.

Laboratory Examination.—The urine, on April 16, 1929, was amber, clear, with a specific gravity of 1.022, and alkaline. It showed no albumin and no sugar or diacetic acid. A sediment contained amorphous phosphates. The Wassermann reaction of the blood was negative on March 17, 1929. Red blood cells numbered 4,470,000; the hemoglobin content was 60 per cent. The white blood cells numbered 5,250, of which 72 per cent were polymorphonuclears, 24 per cent lymphocytes and 4 per cent transitionals. On April 4, 1929, roentgenologic examination of the chest revealed enlarged hilar glands, particularly at the right hilus, and infiltration of the right upper lobe (Dr. L. Bryan).

The working diagnosis at this time was that there existed a tumor of the chest, with axillary metastases.

Pathologic Examination.—On May 2, the left axilla was opened in the hope of removing a large lymph node for pathologic examination. My associates and I were surprised to find, on dissection, that the numerous masses in the axilla were not nodes, but varices of the axillary vein. However, a small node was removed, and the following pathologic report was obtained.

Examination of the lymph node showed only chronic lymphadenitis. The germinal areas were normal. The sinuses were dilated; the blood channels were engorged; the reticular tissue was thickened, and there was some transudation of blood into the pulp. There was no evidence of malignant growth, Hodgkins' disease or lymphosarcoma or tuberculosis.

Diagnosis.—The diagnosis was chronic lymphadenitis.

Therapy.—Bronchoscopic examination was considered at this time, but deemed inadvisable because of the marked edematous infiltration of all the structures of the neck. So it was decided to subject the patient to deep roentgen therapy in the hope that in spite of the observations to the contrary, the new growth might be of lymphatic origin and therefore respond to such therapy. Hence the patient left the hospital and reported back at intervals for therapy.

Second Admission.—On April 15, 1929, the patient returned to the hospital for further study. There had been no change symptomatically or objectively. The results of physical examination were as before, and the roentgen therapy had produced no noteworthy alteration in the suspected new growth. Obstruction to the superior vena cava was now suspected.

Roentgen examination of the chest was repeated, bronchography with iodized poppy seed oil 40 per cent was done, studies of the esophagus with a thick barium sulphate meal were undertaken and an electrocardiographic examination was made. The results of these examinations were reported as follows:

Roentgen Examination.—On April 22, roentgenograms of the chest, anteroposterior and lateral views, with iodized oil demonstrated normal bronchi at the right base. There was an infiltrating lesion extending out from the right hilus. Probable malignant growth was shown. (Dr. L. Bryan). On April 27, a roentgenogram of the chest after a thick barium sulphate meal showed no abnormality of the esophagus and no evidence of aneurysm. (Dr. Levitin.) On April 29, roentgenograms of the dorsal spine, anteroposterior and lateral views, showed marked hypertrophic changes about the middle and lower thoracic vertebrae due to hypertrophic arthritis. (Dr. L. Bryan.) On May 2, roentgenograms of the skull, lateral, anteroposterior and postero-anterior views, were negative. (Dr. L. Bryan.)

Electrocardiographic Examination.—On May 3, electrocardiographic examination by Dr. J. J. Sampson showed that there was little shift of the electrical axis, suggesting that there might be adhesive pericarditis.

Third Admission.—Again, on May 24, the patient was readmitted, complaining of severe attacks of dyspnea and an increasing nonproductive cough. He had fainted twice while out of the hospital.

Physical Examination.—The essential physical observations at this time were as follows: The pupils were equal and regular and reacted normally to light and in accommodation. The fundi showed marked distention; the nerve head was edematous. The trachea was in the midline. There were no palpable glands. The neck was markedly swollen, and the jugular veins were distended. There were numerous distended veins and venules over the anterior surface of the chest. Expansion was limited at the right apex. There was slightly increased vocal fremitus at the apex of the right lung anteriorly. Percussion showed diminished resonance over the whole chest, but was from dull to flat at the right apex anteriorly and at both posterior bases. There was distant bronchial breathing at the right apex. Breath sounds were diminished at both bases posteriorly. There were no râles. Ten days later there were signs of fluid at the left base.

Roentgen Examination.—On May 24, roentgenograms of the chest, anteroposterior and lateral views, showed no change since the previous examination. (Dr. Levitin.) On June 4, a roentgenogram of the chest showed grayness at the left base due to a small pleural effusion. The infiltration of the right upper lobe showed no change. (Dr. Levitin.)

On June 13, the patient was allowed to go home at his own request. Fourth Admission: Two days later, he was admitted per ambulance in a semicomatose condition, it being said that he suddenly collapsed on the street.

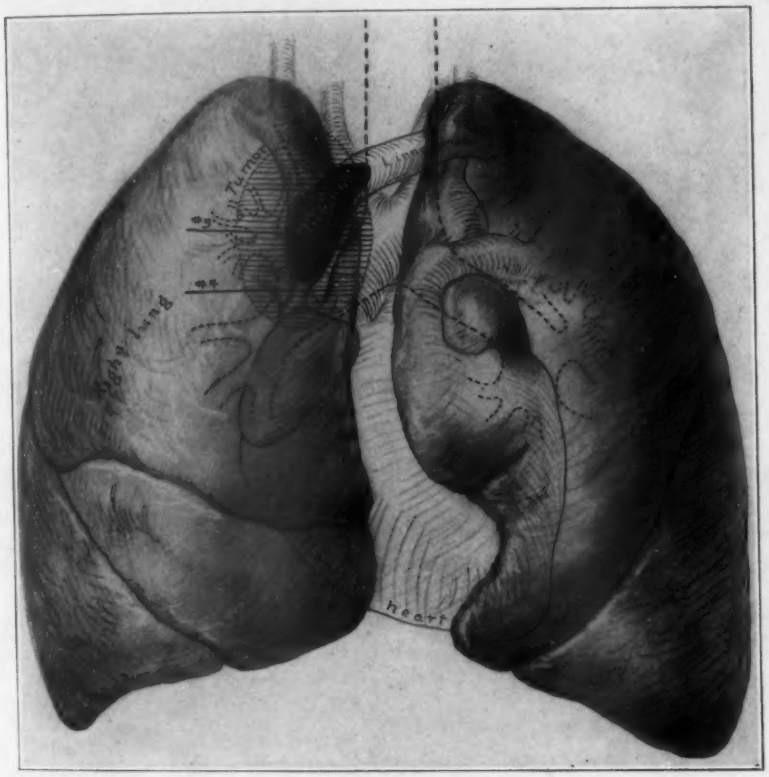

Fig. 2.—Diagrammatic representation showing relative location of the tumor, constriction and obstruction of the superior vena cava and position of the thrombus.

Physical Examination.—The patient was cyanotic, dyspneic, irrational and restless, and showed marked swelling of the neck, with enlargement of the veins of the neck and arms. The skull and scalp were normal. The sclerae were icteric. The retinal veins were engorged. The nose was normal. The lips were dry, and there was a deep furrow in the lower lip. The breath was foul.

The respirations were increased to 30 per minute and were shallow, with a rattling noise in the larynx. The wall of the chest was covered with distended and dilated vessels. The anterior surface of the left side of the chest was deeply colored with a brown pigmentation. The right side of the chest was dull through-

out anteriorly and posteriorly. The left side of the chest was dull anteriorly and resonant posteriorly. The breath sounds were vesicular, but on the right side they were markedly diminished in both the front and the back. The heart sounds could not be heard because of the noisy respiration due to laryngeal noise.

The abdomen was normal. The liver and the spleen were not felt. There was an indirect incomplete inguinal hernia on the left side.

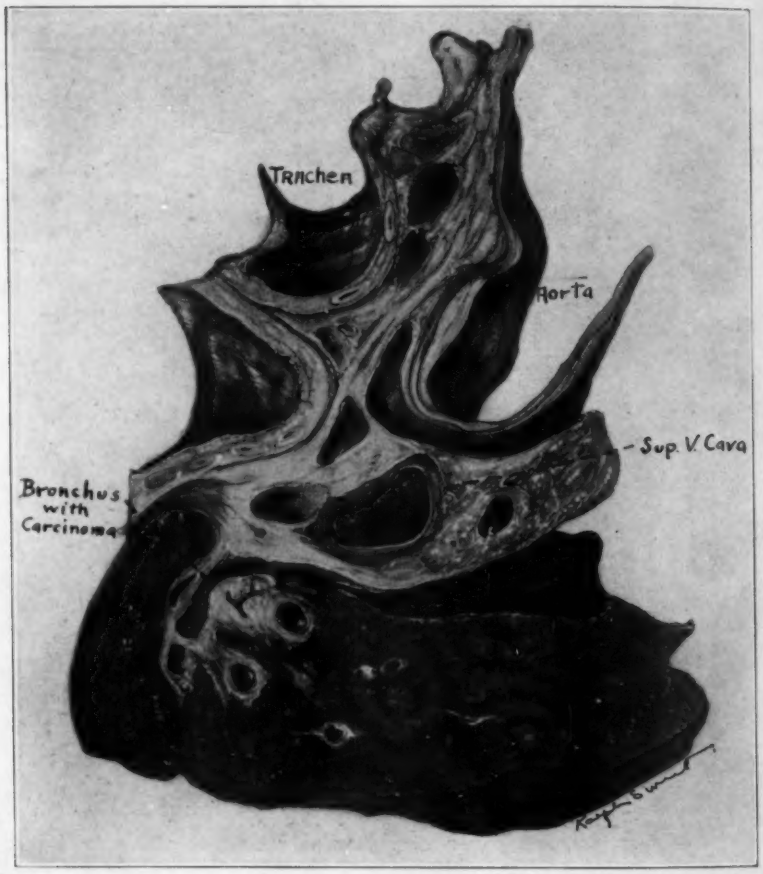

Fig. 3.—Cross-section of the right upper lobe at the level shown in figure 2, showing peribronchial involvement and thrombus in the superior vena cava.

The extremities were wasted. There was an ecchymotic swelling on the dorsum of the right hand and on the right elbow. The reflexes were normal.

The pulse rate was 92, the respirations were 26 and the temperature was 36.8 C. (98.2 F.).

The patient was given one-sixth grain of morphine and one-one hundred and fiftieth grain of atropine, and shortly thereafter he went to sleep. One hour later, the pulse rate was 116 and the respirations 32. Fifteen minutes later, the patient had quietly expired.

Anatomic Diagnosis.—The anatomic diagnosis was as follows: carcinoma with peribronchial distribution at the root of the right upper lobe, extension into the adjacent mediastinal tissues, with marked stenosis of the descending vena cava and metastasis to the right suprarenal gland; purulent bronchitis of the right lung; slight pleural transudate in both cavities of the chest; acute splenic tumor; parenchymatous degeneration of the viscera, and thrombosis of the superior vena cava.

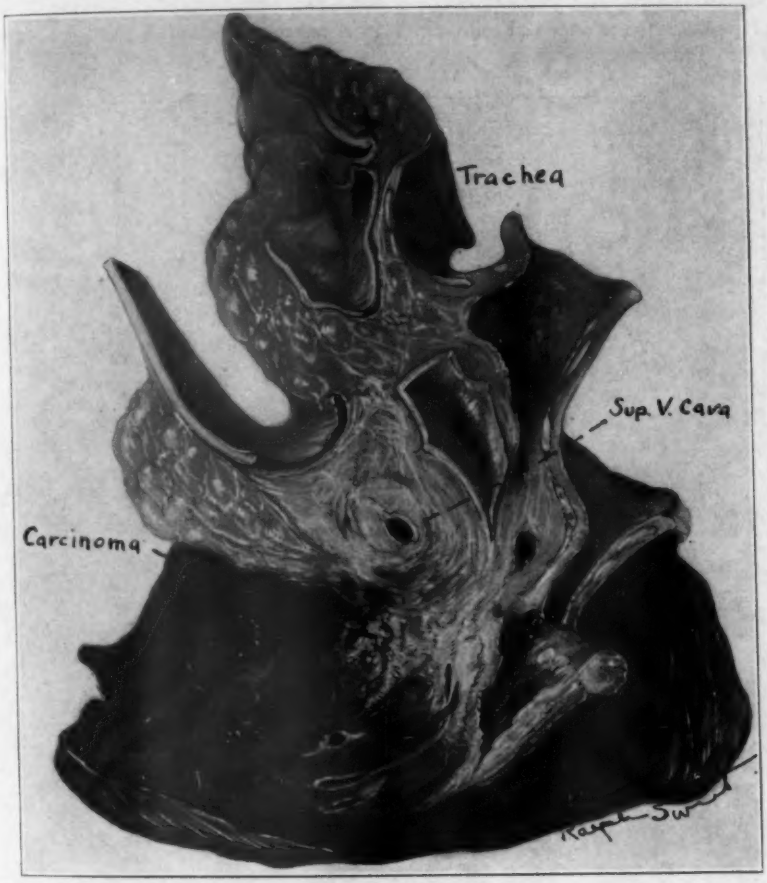

Fig. 4.—Cross-section of the right upper lobe at the level shown in figure 2, showing the constriction of the superior vena cava and malignant infiltration.

Autopsy.—The postmortem observations, as reported by Dr. G. Y. Rusk, were as follows:

The remains were those of a moderately undernourished man, appearing to be about 60 years of age. Rigor mortis was passing off. There was moderate postmortem lividity. The pupils were circular, equal and midwide. The eyes showed internal strabismus. The neck was thick, with deep-seated induration, but without any palpable nodules. The axillary nodes were moderately enlarged, slightly more so on the left. The inguinal nodes were nodular and somewhat increased in size, more so on the right. The abdomen showed an old, well healed

site of incision for appendectomy. There was no edema of the extremities. The left side of the chest showed an extensive mottled hyperemia.

When the usual median incision was made, the subcutaneous tissues over the sternum were edematous; those of the abdominal wall were normal. The right side of the chest contained about 300 cc. of transudate. The left lung showed scattered chronic adhesions over the apex and on the posterior and mesial surfaces of the upper lobe. There was about 200 cc. of transudate in the left side of the chest. The pericardial cavity was normal. The peritoneal cavity showed chronic perisplenic adhesions and chronic villose adhesions about the region of the appendectomy.

Fig. 5.—Photomicrograph of the lung and bronchus, showing the tumor lifting up and penetrating the bronchial mucosa (from the left).

The heart was of normal size. The tissues were moderately softened, apparently from postmortem alteration. The endothelium of all the chambers, including the valves, was normal. The first portion of the aorta was normal. The myocardium was somewhat pale, cloudy and softened; no areas of fibrosis were seen. The coronary vessels were essentially without changes.

The left lung showed the usual pigmentation to a moderate degree. The right lung was removed, with the pericardium and the mediastinal contents. On introduction into the superior vena cava, a probe about 2 mm. in diameter met with distinct resistance about 1 cm. above the pericardial opening. The right lung was of normal size. At the inner aspect of the upper lobe near the hilus, there was an ill defined palpable mass that felt denser in the adjacent mediastinal tissues.

A section of the trachea and bronchi to the upper lobe showed the mucous membranes hyperemic. No ulceration of the mucous membrane was seen, but encircling the bronchus of the upper lobe was a layer of dense white tissue varying in thickness up to about 2.5 mm., fairly localized on the pulmonary side, but continuous with a nodule, about 2.5 cm. in diameter, that extended into the mediastinum. Through the center of this nodule ran the markedly stenosed superior vena cava. Beyond the growth in the pulmonary tissues there was a thin, mucopurulent exudate. The encircling of the bronchi by the growth, while making the walls rigid, apparently caused no appreciable narrowing of the lumina. Section of the lower lobe showed hypostasis and mucopurulent exudate in some of the larger bronchi.

Fig. 6.—Photomicrograph of the tumor tissue, showing the tumor to be composed of large and small cells growing usually in columns in a stroma of dense fibrous tissue.

The spleen was increased to about twice its normal size and was soft. The capsule was torn in several places, the sites of adhesions. On section, the tissues were grayish red and soft, and the anatomic details were obscure.

The liver was of normal size. On section, it showed slight cloudy swelling, but was otherwise normal.

The right suprarenal gland was moderately enlarged. On section, it showed a firm, white, irregular mass of tissue that was apparently a metastasis from the carcinoma. The left suprarenal gland was normal.

The kidneys were moderately reduced in size. The capsules stripped with moderate readiness. On section, there was some increase in the peripelvic fat. The tissues were somewhat grayish, but the architecture appeared fairly well preserved.

The gastro-intestinal tract was normal; the urinary bladder and prostate were normal, and the pancreas appeared to be normal. The retroperitoneal lymph nodes were soft and hyperemic. The abdominal aorta showed a moderate amount of atheroma without ulceration or calcification.

The central nervous system was not examined.

Sections of the superior vena cava showed a definite thrombosis with considerable organization. The process must have been of at least several weeks' duration.

Histologic Examination of the Tumor.—Histologic examination of the tumor by Dr. Zera E. Bolin showed that it was composed of large and small cells usually growing in columns in a stroma of dense fibrous tissue. The cells varied from round to oval, unless compressed; in this case they were spindle-shaped. The nucleus was oval and stained deeply. Many mitoses were seen and a moderate number of atypical mitoses. The protoplasm was eosinophilic. In lymph nodes and other places where there was but little pressure, the cells tended to arrange themselves in small alveoli. There were, as a rule, from four to eight cells in a group. No cilia could be found in these alveoli, nor could any evidence of secretion be found. The fibrous stroma was dense and made up about two thirds of the tumor. A moderate number of mononuclear cells were found in the stroma.

Histologic Diagnosis.—The histologic diagnosis was scirrhous adenocarcinoma of the lung.

DISRUPTION OF PELVIS WITH LUXATION OF THE INNOMINATE BONE*

C. W. PEABODY, M.D.
DETROIT

Eight patients have been received in the Henry Ford Hospital with unusually severe injuries to the pelvis, all sustaining a complete disruption of the pelvic bone with separation and displacement of one side from the other. In five instances there was separation and displacement anteriorly at the pubic symphysis, with accompanying separation and displacement of one or both sacro-iliac synchondrosis, constituting a true dislocation or luxation of the innominate bone. In the others, instead of separation at the pubic symphysis, there were vertical fractures close to it, with accompanying rupture of the sacro-iliac joint and upward displacement of what was practically the whole innominate bone, making the injury a comparable one. Several patients had accompanying fractures at other points in the pelvic ring but with little or no displacement at these points, so that the most striking lesion seemed to be the displacement of the innominate bone as a whole. One of these patients died, one was not traced, and the rest made a complete recovery.

As seven of these patients came under my care in the space of six years in an institution which has comparatively few cases of major accidents (on the average not more than a dozen beds being occupied in this period by patients with fractures), I gained the impression that this must be a not uncommon type of pelvic injury. Reference to the literature to determine the usual outcome and prognosis, on the contrary, seemed to warrant a conclusion that this was an infrequent lesion, and that the outlook was usually serious.

In using the title "Luxation of the Innominate Bone" to designate this type of injury, I have taken what seemed the most suggestive anatomic expression. In the literature, however, this term has been used but few times, the main terms employed being pelvic luxation, separation or displacement. Some of these cases have been recorded as sacro-iliac separation and a few as separation of symphysis pubis, and this confusion in indexing with simple luxations of the front or back alone added much to my labor. The German terminology is fairly uniform (incidentally German references comprise a total in excess of all others combined), the term "Luxationen Beckenhafte" usually obtaining.

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* From the Orthopedic Division, Department of Surgery, The Henry Ford Hospital, Detroit.

* Presented originally at Detroit meeting of Central States Orthopedic Society, November, 1927.

Only a few instances of triple separations have been reported, that is, separation of both sacro-iliac bones as well as an anterior rupture.

References in the literature go back over one hundred years. During this period probably no more than sixty-five cases have been reported, usually as single instances, a few writers reporting two, one four and one six; but this has been the highest personal observation, with the exception of observations on eighteen summarized by one author, six of these being fresh injuries and nine old injuries with persisting displacement. The rapidly increasing observations of the last two decades have certainly established this injury as fairly frequent and as bearing a favorable prognosis. This is in contrast to the attitude of earlier times, when most of the reports were of fatal cases.

In the diagnosis of this lesion it has not been necessary to use roentgenograms, except for confirmation. Serious injury to the pelvis is almost immediately suggested by the complete helplessness, severe shock, the great pain referred to pelvis on any movement, the tenderness on palpation of the synchondroses, and the gross hypermobility of the pelvis to manipulation, if examination is carried this far. In the cases in this report the diagnosis of severe pelvic injury was always made by a senior intern on first examination, and immobilization of the pelvis by a binder and Bradford frame was secured before anything else was done. The degree of hypermobility was appreciated only at the time of reduction under an anesthetic.

The injury seems uniformly to be accompanied by severe initial shock, but rarely by visceral complications. In few of the cases were the latter important; but in most the symptoms of shock were rather prolonged, delaying any vigorous measures of reduction. Fracture, usually without displacement, at some point in the pelvic ring frequently accompanies the innominate luxation, but has seemed to be a less important factor and of little importance as a complication, displacement at the fracture line being slight. Fracture of the lateral process of the fifth lumbar vertebra is also seen in combination. This last accompanying pelvic injury has been illustrated by me in the past.[1] In all the cases in the present series, accompanying fractures of one or another of these types was present.

Although the mechanism of innominate dislocation has generally been considered to be a crushing injury, the victim being squeezed or rolled, with probably a large majority of reported cases having been caused by an accident of this nature, a considerable number have been produced by a straight fall. The series reported here is divided between these types of violence. Nor does either type seem to have a consistent influence on the character of the luxation, i. e., whether it is a simple proximal or posterior displacement of one half of the pelvis or luxation accompanied by excessive rotation.

1. Peabody, C. W.: Unusual Fractures, J. Bone & Joint Surg. **4**:459, 1922.

With or without complete reduction, ankylosis of the involved synchondroses seems invariably to occur. The union at the sacro-iliac joint is usually bony. This seems to confirm observations of many that any extensive traumatic displacement of a sacro-iliac joint will be followed by ankylosis. Although recovery has been found to follow frequently without reduction, the latter seems necessary for complete freedom from disability. Either a scoliosis or a raised shoe are inevitable without more or less complete reduction of any considerable displacement. In most reported cases reduction has been gradual, being obtained by weight extension of the shortened limb, by countertraction and by circular compression of the pelvis. In others, particularly in German cases, reduction has been obtained by manipulation under an anesthetic, followed by retention with a plaster of paris cast; this has sometimes been resected a little in midline and further reduction secured by turnbuckles placed in either a transverse or an oblique position as indicated. Severe discomfort has usually been reported during gradual reduction.

A method of treatment was successfully used in most of the nonfatal cases in this series which is a little different from the methods reported. As soon as the general condition warranted the use of an anesthetic (from a few days to several weeks), the patient was moved on his frame to the x-ray department and placed on the tilting fluoroscopic table used for gastro-enteric observations, the patient's feet being placed at the head end of the table. The foot on the displaced side was made fast to the head of the table, and with anesthesia induced, the mobility of the pelvic girdle was verified by palpation. With the body steadied by the operator and assistant, the table was then tilted nearly to the vertical position, the weight of the body coming finally entirely on the fastened leg. Under fluoroscopic control, the pelvis was very gently manipulated between the hands until replacement could be seen as well as felt; a previously prepared webbing belt was at once placed around the pelvis and buckled tight; the table was returned to the horizontal position, the traction released and the position again checked by the fluoroscope. Where rotary displacement was present, the limb on the anterior side was held down, while the opposite limb, extended at the knee, was strongly flexed at the hip, levering this side of the pelvis forward. When the patient was returned to his room, the Bradford frame, to the end of which the patient's foot was reattached, was left inclined head down. Plaster of paris was not used. To guard against reluxation in bed, 20 pounds of traction was maintained on the leg of the affected side. The binder was replaced for greater comfort by the overhead pelvic sling after return to the fracture bed. In two cases a recurrence of some of the rotation displacement at the symphysis occurred in the second month. In both instances the patient had to be transferred to another wing, being removed from bed for this purpose, and although a tight binder is said to have been applied, no control

roentgenograms were obtained for some time afterward. On account of probable infiltration of the soft tissue at the pubis, operation with wiring was then done; little mobility at the back of the pelvis could be obtained at that time.

In case 1, taken from the earlier hospital files, operation performed early by Dr. R. D. McClure, with manipulation of the pelvis, wiring of the symphysis and fixation in plaster gave a highly satisfactory result. In this case there was no fracture on the displaced side; direct manipulation of the anterior end of innominate bone would probably be effective in reducing displacement in this type of case when early operation is possible. In another case in this series the patient suffered relatively slight displacement posteriorly although there was complete rupture of the sacro-iliac and marked displacement at the symphysis. There was an accompanying ruptured bladder, for which early operation was done. No definite manipulative measures were carried out, yet subsequent roentgenograms showed that both luxations had been spontaneously reduced. This was maintained by treatment on a fracture bed until consolidation was complete.

Of the eight patients seen, six were treated to a conclusion. One case was fatal before any definite treatment for skeletal injury could be carried out, and one patient was removed from the institution shortly after admission. In the six concluded cases, all the patients recovered without any residual disability referable to the pelvic injury. In all the upward displacement of one side of the pelvis was corrected, and consolidation of the pelvic ring was obtained. In two, the relations at the symphysis were not entirely normal, and anatomic reposition at the points of fracture was not obtained.

It may be of interest to note that sciatic pain was not a marked symptom, save in the cases showing an accompanying fracture of the lateral process of the fifth lumbar vertebra.

The roentgenograms here shown do not include the first case, in which examination was made on glass plates that are no longer preserved. The same is true for case 2, except that on a recent return of this patient for another condition a roentgen examination was obtained and is here shown. The remaining six cases are illustrated by roentgenograms taken before and after treatment.

REVIEW OF THE LITERATURE

The well known textbooks in this country dealing with fractures, such as those of Wilson, Cotton, Scudder and Stimson, give rather scant attention to the injury under discussion. Wilson, under the title "Separations of the Symphysis," emphasized that this condition must be accompanied by some degree of sacro-iliac luxation if fracture has not occurred, and in discussing sacro-iliac dislocation stated that in complete

dislocation symphyseal separation must have occurred though not showing. The entity of a complete innominate dislocation is not mentioned.

Cotton dealt with this subject under the title "Fractures" rather than "Dislocations," and following a paragraph on "Separation of Symphysis" there is a diagram illustrating a coincident sacro-iliac luxation. The author stated that this double, or even triple, dislocation may occur but must be rare. He stated that there are cases on record, and that the lesion is not as serious as one would expect. One roentgenogram is reproduced showing a complete upward dislocation of one innominate bone accompanied by fracture of the acetabulum; a note reports complete recovery without disability at the end of one year.

Stimson recognized the occurrence of complete luxation and mentioned in addition the universally quoted cases of Malgaigne, Salleron and Creite, also one by Earle in 1835, not elsewhere referred to. He seems to imply that the condition is rare and says: "As a rule prognosis is extremely grave."

Scudder, in a recent edition (1928), failed to mention this injury, either in the extensive chapter on fractures of the pelvis, or in the supplement on dislocations.

Case reports of this injury go back to 1820 with a report by a Belgian surgeon, Cloquet. Malgaigne, in 1855, reported six cases with four deaths. Salleron, in 1871, reported four cases, all fatal. Other case reports up to 1900 were single ones totaling twenty-two. Since the beginning of the twentieth century, the cited cases have been more numerous, but still consist of only single instances or of two cases, with the exception of a contribution by Haumann, who reported six new cases not noted previously and mentioned also a personal observation of nine additional patients that he had seen some time after injury but who showed persisting displacements. The total since 1900 is forty-one, making in all sixty-three. The accompanying table illustrates the chronological incidence.

Special additional mention should be made concerning some of the contributions. In 1925, Maisonnet had a detailed and interesting paper in the *Paris médical* in which pelvic injuries suffered by horsemen either from shock in the saddle or by fall to the ground are discussed as to the result to be expected from either, and particularly the urinary complications of pelvic injuries. This was apropos of his own cases of innominate luxation in which there was serious urethral and bladder injury but ultimate recovery with moderate disability despite persisting displacement which he considered rather common. There is an extensive bibliography. In the report of Haumann, it is noted that in nine of his whole series there was some type of fracture in addition to the dislocations, six patients having this in the same half of the pelvis and three in the opposite half. This did not appear to have complicated the original or final state. All showed a favorable outcome with recovery,

the shortest duration being one month and the longest seven months. In some of the ancient cases observed by him the luxation had been neither recognized nor corrected, but invariably had consolidated. Scoliosis was usually present in these, but to a marked degree in only three. One of the patients in the new series died on the ninth day and another in the eighth month from urinary complications. Of the total number, eight returned to full earning capacity, three others had 10 per cent disability and the remainder 25 per cent, which was the

Chronological Table

Date	Name	No. of Cases
1820	Cloquet: Nouv. J. de méd., vol. 7, p. 201	1
1835	Earle: Med. Chir. Tr., vol. 19, p. 257	1
1849	Thouvenet: Bull. Soc. anat. de Paris, vol. 24, p. 29	1
1850	Parmentier: Bull. Soc. anat. de Paris, vol. 25, p. 35	1
1855	Malgaigne: Traite des Luxations, Paris	6
1865	Larry: Gaz. d. hôp., p. 135	1
1868	Dolbraux: Gaz. d. hôp., vol. 41, p. 135	1
1871	Salleron: Arch. gen. de méd. Paris, vol. 3, p. 34	4
	Dubreuil: Gaz. d. hôp., vol. 44, p. 413	1
1875	Dupont: Arch. méd. belges	1
1872	Pollock: Lancet, vol. 2, p. 409	1
1888	Niehaus: Deutsch. Ztschr. f. Chir., vol. 27, p. 467	1
1890	Hallowell: Northwest. Lancet, vol. 10, p. 135	1
1899	Hopkins: Ann. Surg., vol. 29, p. 601	1
	Total prior to 1900	— 22
1902	Linser: Beitr. z. klin. chir., vol. 35, p. 94	1
1903	Riedinger: Arch. f. Orthop., vol. 1, p. 414	1
1905	Tillmanns: Ber. d. deutsch. chir. Gesellsch., Stuttgart	1
1906	Creite: Deutsche Ztschr. f. chir., vol. 83, p. 391	1
	Stinelli: Cong. d. soc. Ital. d. chir., Milan, vol. 19	1
1908	Grimbach: Deutsche Ztschr. f. chir., vol. 94, p. 609	1
	Lindenstein: Beitr. z. klin. Chir., vol. 58, p. 709	1
	Warrack: Brit. M. J., vol. 1, p. 203	1
1909	Felten: Hildebrands Jahrb. der chir., p. 1150	1
	Fischer: Zentralbl. f. chir., 1909, vol. 38	1
1911	Finsterer: Deutsche Ztschr. f. chir., vol. 110, p. 191	1
	Guibé: Bull. et mém. Soc. Anat. de Paris, vol. 86, p. 36	1
1914	Heinemann and Siedamgrotzky: Arch. f. klin. Chir., vol. 103, p. 927	2
1917	Webb and Snell: Arch. Rad. & Elec., vol. 2, p. 33	1
1918	Simpson: Ann. Surg., vol. 67, p. 348	1
1919	Hirschberg: Deutsche med. Wchnschr., vol. 33, p. 904	2
1920	Block: Deutsche Ztschr. f. Chir., vol. 160, p. 113	1
1921	Berard: Lyon chir., vol. 38, p. 1	2
	Haumann: Beitr. z. klin. Chir., vol. 103, p. 278	6 recent 9 old
	Moritangard and Moreau: Rev. d'orthop., vol. 8, p. 415	1
1923	Hermansdorfer: Deutsche Ztschr. f. Chir., vol. 183, p. 129	2
1923	Cotton: Dislocations and Joint Fractures, Philadelphia, W. B. Saunders Co.	1
1925	Marisonnet: Paris méd., vol. 2, p. 161	1
	Total since 1900	— 41
	Writer's series	8
	Grand total	71

maximum. Roentgenograms showing typical displacement were included in the six cases in which treatment was given.

Hermansdorfer's report in 1923 contained an excellent clinical report of observations and treatment in two cases, with roentgenograms of one. Complete recovery was reported in both, one patient being treated by a spica-jacket cast with the midsection removed down the front and obliquely placed turnbuckles used to reduce the displacement, and the other by early manipulation followed by traction and countertraction in bed and finally the same cast technic. Reduction was not entirely

complete in either case, although solid fixation occurred. The author discussed the previous literature and methods of treatment used by others in his country. Gradual reduction by traction and compression seemed to be more favored than early manipulation, which was held dangerous. He quoted Block as using skeletal traction.

Simpson reported one case with complete recovery after hospitalization of ten weeks and disability over one year. Early reduction by manipulation was carried out, and the symphysis was wired. Reduction was found to be incomplete but was later improved by longitudinal traction and lateral cross-traction through windows in the cast that had been applied at operation. His patient had no fractures accompanying the dislocation. He reviewed previously reported cases in which there had occurred nothing but the innominate luxation; he found twelve such instances with a mortality of 25 per cent. In five of the twelve, however, no roentgen evidence had been obtained to rule out the fractures commonly observed by others.

Block, after reporting the critical case of a boy 9 years of age who had a complicating perforating wound of the abdomen but recovered with incomplete reduction and some disability, discussed the subject in some detail, including five other cases in the literature since Finstein's report in 1911, one of which he insists must be discarded.

In 1911, Guibé reported in some detail the observations in a fatal case. He also critically reviewed the previous literature, particularly Tillmanns' previous review of eleven reported cases, and, having analyzed these, discarded many for various reasons and held that there were only eight authenticated cases prior to his own, all fatal. Apparently he was unwilling to accept any criteria of diagnosis save autopsy observations.

Finsterer, in an excellent discussion following his own case report of a boy of 12 who made a complete anatomic as well as functional recovery despite a lapse of two weeks before treatment (traction followed by wiring), searched the literature subsequent to Tillmanns' review in 1905 and found eight additional case reports.

Creite, in 1906, further emphasized the earlier ideas that this injury is rare. Though his own cases were fatal, with severe infection in perineal lacerations, he expressed the belief that without such complication there should be a very low mortality rate.

The older single reports were almost invariably of fatal cases; of Malgaigne's six, four were fatal, and of Salleron's four, one was fatal.

In seeking conclusions from the literature in general, it may be said that as increasing attention is paid to its possibility, complete dislocation of the innominate bone is being observed more often, and more frequently in nonfatal cases; that though the roentgen examination does not seem necessary for diagnosis, increasing recognition of the condition has followed the wider availability of this method of study; that though

the mechanism seems to be more frequently a crushing injury, the displacement can be produced by a severe fall, which, however, is more frequently immediately fatal and so diminishes the likelihood of clinical observation. Without visceral complications, recovery from this unilateral pelvic dislocation can uniformly be expected with or without treatment. Reduction is likely to decrease disability. Reposition is more complete if the procedure is not too long delayed, and manipulation under an anesthetic, if carefully carried out, does not seem to increase the mortality. A review of the literature would seem to indicate that there should be a more extensive recognition of the condition in the textbooks than now prevails.

CONCLUSION

Eight acute cases of traumatic dislocation of the innominate bone, with one fatality, are reported. A safe method of early reduction by manipulation is described and recommended. A fairly comprehensive review has been made of the literature, which, while probably not absolutely complete, is adequate enough to emphasize the clinical importance of this injury and to allow some general conclusions to be made.

REPORT OF CASES

CASE 1.—Peter H., a stonecutter, aged 24, was admitted to the hospital on the evening of Nov. 11, 1917, a few minutes after being crushed between a standing and a moving truck. He was conscious at examination and was in great pain referred to the pelvis; this pain became intolerable if the body or limbs were handled. There was marked rigidity of the abdominal and lumbar muscles. He was in a state of considerable shock, with thready pulse, clammy skin, and a blood pressure of 90 systolic and 56 diastolic. The greatest tenderness was noted in the region of the left sacro-iliac joint, of the symphysis and of the perineum, where separation and displacement could be readily appreciated by palpation. Rectal examination did not suggest urethral injury. There seemed to be shortening of the left leg. There was also long, deep laceration down the adductor aspect of the thigh.

Simple cleansing was administered to the wound with sterile dressings, and after the patient was strapped to a Bradford frame, treatment was restricted to combating the shock, which persisted for about three hours. Bloody urine was obtained by catheter the first night, and on tentative diagnosis of a ruptured bladder a retention catheter was inserted. The next day only occasional blood cells were present in the urine. The catheter was withdrawn, and voiding became spontaneous.

Roentgen examination of the pelvis was made on the day after admission. Glass plates were being used at that time and none of these has been preserved. Accordingly, the roentgenographic interpretation is quoted in detail: "The left side of the pelvis does not seem to be in the same plane as the right side. There is no line of fracture seen on this side of pelvis. There is apparently an unusually wide separation of the left sacro-iliac joint. There is marked separation of the symphysis pubis about 5 cm., with riding upward of the right side. There is a double fracture of the right descending ramus of the pubis at the obturator foramen with slight displacement. Diagnosis: Fracture ischiopubic right, dislocation sacro-iliac left, dislocation symphysis pubis."

The patient's general condition improved excellently, and though the laceration was slightly infected, it was controlled by Carrel-Dakin technic; a large scrotal hematoma required nothing more than support, and no other complications developed.

On the eighth day, the temperature being normal and the general condition good, persisting dislocation of the symphysis was reduced by open operation with fixation by Lane plates; the pelvis and lower extremities were included in a plaster cast. Convalescence from the operation was entirely uneventful. On the twentieth day, skin was grafted over the granulating wound on the thigh. On the fortieth day, the patient began to sit up in bed, and on the forty-fourth day he was discharged to his home by ambulance.

The patient failed to return for further convalescent treatment or observation, but about three years later responded to a recall letter, reporting in person, in apparent good health and with no obvious disability, stating that he was back at his regular work as a stonecutter. The only subjective symptoms were occasional burning and some pubic discomfort on lifting. Arrangements were made for roentgen examination and physical check up, but he failed to return for this and was not seen again. However, testimony as to the resumption of his former occupation would seem to make the result most gratifying in this case. This patient was under the care of Dr. R. D. McClure, who also performed the operation.

CASE 2.—Charles D., a Jew, aged 57, short and weighing about 190 pounds (86.2 Kg.), hypertensive in type, came under my care on Nov. 5, 1921, having been admitted to the hospital the previous day following an automobile accident. Details of the accident and of the condition on admission were not available. At examination he was found to be in a rather shaky condition, apparently in great pain and a marked state of shock. There were multiple minor cuts and abrasions and a considerable scalp wound, which had been sutured. The pulse rate was increased and the temperature elevated, and the pulse beat was of poor quality. The right side of the abdomen was rigid over the lower half, with generalized distention and tympanites. The scrotum was hemorrhagic, and the size of a large grapefruit; there was a large scrotal hernia on the right. A wide defect was present to palpation at the symphysis. There was great tenderness over the lumbosacral and right sacro-iliac joints, and pressure anywhere on the pelvis was painful. There seemed to be gross abnormal mobility of the right innominate bone with considerable cephalad displacement. The patient had not voided spontaneously, and the urine had been bloody on each catheterization.

A roentgen examination was made on admission. At this time glass plates were being used, which have not been preserved. The detailed report is as follows: "There is a fracture of the right transverse process of the fifth lumbar vertebra with 1 inch upward displacement. There is a dislocation of the sacro-iliac synchondrosis on the right, the ilium being displaced upward about 1 inch, with ½ inch separation of joint surfaces. There is a complete dislocation of the symphysis pubis with 2 inch separation. There is a fracture of the ascending ramus on the right side of the pubis with no displacement and a comminuted fracture of the descending ramus, one fracture line being near the pubis and the other near the ischium, the fragment being displaced considerably downward and backward."

The patient was placed on a Bradford frame, and in addition a canvas hammock-sling with overhead suspension to the pelvis were used. Adhesive traction was applied to the right lower extremity with about 30 pounds weight and elevation of the foot of the bed. Supportive treatment was pushed, and a retention catheter was inserted.

Following these measures there was some improvement in comfort and general condition, and no definite evidence of peritonitis obtained. However, tympanites increased, and a paralytic ileus seemed imminent, only most energetic nursing, with administration of stupes and solution of pituitary finally starting intestinal elimination. It was ten days after admission, however, before this condition was entirely controlled. The principal complaint during this period was intense sciatica on the right side, which resisted the heaviest doses of narcotics and sedatives. A considerable traumatic psychosis prevailed for many days, and the patient absolutely would not tolerate the weight extension, which had to be removed after a few days. Bronchitis was noted a few days after admission and became rather diffuse, but inhalations and the use of blow bottles was pushed, and consolidation did not develop. However, there was indication of a migratory bronchopneumonia

Fig. 1 (case 2).—Roentgenogram made five years after injury. No disability referable to the pelvis. The original roentgenogram of this case made on glass plates was not preserved. See roentgen interpretation in the text. First examination showed 1 inch upward displacement of the innominate at the right sacro-iliac joint and 2 inch separation at the symphysis. Note the fusion of the right sacro-iliac with little residual displacement. Originals of this print show some bony continuity across the front of the pelvis, not obvious in the print.

with fluctating temperature and respiration prevailing for the first four weeks. For the first two weeks, the temperature ranged from 99.5 to 103 F.; and in the ensuing fortnight between normal and 101 F. The pulse rate followed the temperature, ranging between 100 and 120. During most of this period, the patient was on critical list.

One month after admission, clinically there seemed to be persisting innominate dislocation and a continued complaint of sciatic pain. A portable x-ray apparatus was not then available, and it had not been felt safe to move the patient.

On the thirtieth day after admission, his general condition being fairly satisfactory and the condition of the chest clearing up, he was sent for further roentgen examination, being moved on a Bradford frame with a canvas corset to the pelvis. Roentgenograms showed little change, save for some decrease in the pubic separation.

The patient and his family were then told that without operation there would probably be continued pain, disability and invalidism, but that operation entailed considerable inevitable risk. It was decided to accept this risk, however, and at the end of the fifth week, closed reduction was performed under ether. The method was that described elsewhere in this article.

Postoperative convalescence was unexpectedly good, no pulmonary complications following. A cast was applied, making it possible to turn the patient completely over, which helped in this connection. On the other hand, the tendency to distention recurred about a week after operation, and continued to be a problem until the cast was removed at the end of three weeks. Four weeks after operation he began to sit up in bed, and two weeks later in a wheel chair, with a webbing belt. An annoying complication about this time was a severe edema of the lower extremities, without nephritic symptoms; on the right side, the edema almost had the aspects of an elephantiasis. It was followed by severe arthritic disturbances in all these joints that proved extremely resistant to physical therapeutic measures. Three months after reduction and four months after admission, the patient began to use crutches, but he did not leave the hospital for another month.

The postoperative and final roentgen examinations showed fairly complete reposition of the right innominate bone.

The patient did not report again for four months, at which time he was still using crutches but was able to walk about the room easily without them. He laid his difficulty to stiffness and weakness of the knees and ankles. Bony relations at the symphysis and sacro-iliac joints seemed normal, and manipulative tests were negative. There was considerable limitation of motion of the lower part of the back. Nine months after injury he was getting about more comfortably with a cane, and the joints were less swollen and their movements less limited. He reported occasional attacks of mild sciatic pain. No further observations were obtained at that time, but friends reported a year later that he had gone back to work.

Recently he returned for repair of a scrotal hernia. Considerable disability had persisted from arthritic symptoms in the knees, ankles and feet, but he had no symptoms referable to the pelvis. He was able to walk moderate distances, using a cane on account of lameness in the knees. He could bear his entire weight on either limb without any discomfort around the pelvis. There was considerable limitation of motion of the lumbar spine, but no further complaint of sciatica. No mobility at the symphysis could be made out on manipulation. Roentgenograms obtained at this time are here shown.

CASE 3.—James H., a truck driver, aged 31, on April 20, 1924, was caught between his machine and a moving freight car, with injuries to the region of the pelvis. He was rendered helpless and brought to the hospital by ambulance about one and one-half hours after the accident. On admission, he was in a state of moderate shock, but he rallied very quickly. He complained of great pain in the low part of the back and in the front part of the pelvis, which was increased by any pressure on the pelvis or movement of the hips. He was unable to move either hip actively. There were great tenderness and some deformity in the pubic region. There was a definite left inguinal hernia of long standing. The patient was placed on a Bradford frame with pelvic swathe and given moderate supportive treatment.

Roentgenograms then obtained showed slight separation without displacement of the pubis and a longitudinal fracture through the body of the right pubic bone with 1 inch separation; an oblique fracture across the body of the right ilium, and moderate separation of the right-sacro-iliac joint; fractures of both rami of the left pubic bone near the symphysis, with slight separation, marked separation and dislocation of the left sacro-iliac joint.

He voided normally during the night without blood in the urine, and no complications developed in the ensuing days. On the fourth day after admission, closed reduction was performed under ether anesthesia. The method described elsewhere was again used, and it is of importance to note that with removal of the binder and manipulation of the pelvis, a much wider separation of the pubis became palpable and was fluoroscopically observed than was apparent in the original x-ray films taken after the frame and swathe had been applied. The separation of the right sacro-iliac joint did not seem to be accompanied by any displacement, and manipulation was confined to reduction of the displaced right innominate bone.

When the patient was returned to his room, the foot of the bed being elevated, adhesive traction was applied to both lower extremities, with a 20 pound pull on each leg. A hammock sling was placed around the pelvis with overhead suspension of the same amount. No complications followed the operation, and the patient reported complete relief from pain.

Traction on the legs was gradually decreased after the first week and discontinued at the end of the four weeks, reduction being maintained by the hammock suspension. This was discontinued at the tenth week, a webbing belt being substituted, and the patient started to sit up in bed. He was allowed in a wheel chair in the twelfth week and on crutches soon after. He was walking the length of the corridor without discomfort four months after the injury. Discharge was authorized at this time, but the patient elected to have an operation for hernia before leaving, and was transferred to the department of general surgery for that purpose, leaving the hospital three weeks later.

This man proved rather slow in returning to work, which he did not do until six months later; he complained a good deal during that period of symptoms of vasomotor disturbance in the right foot and leg. This responded gradually to physical therapy. One year after the accident, while still holding a light job, he was reported as covering a golf course without symptoms on holidays, and he was put back on full duty. Everything was satisfactory until eighteen months after the injury, when he returned with symptoms of lumbar arthritis. These cleared up when some severe oral sepsis was cared for. Roentgenograms obtained one year after injury showed definite fusion of the left sacro-iliac joint and suggestive fusion of the right joint.

Case 4.—George R., a French-Canadian laborer, aged 18, of slight build, on May 3, 1926, fell 125 feet from a scaffold. Near the ground the boards of a light staging broke the full force of his fall as he crashed through them to the concrete surface below. He reached the hospital in fifteen or twenty minutes. He was unconscious on arrival, and was stuporous for forty-eight hours. No signs of fracture of the skull appeared, but he was in an extreme condition of shock. On admission, blood pressure was 60 systolic. Obvious disalinement of the pelvis led to immediate fixation with the binder and Bradford frame without more detailed local examination. There were abrasions but no lacerations, and no definite evidence of visceral injury, though the abdomen was very rigid in the lower half. This, however, led to catheterization as there was a possibility of a ruptured bladder. Three hundred cubic centimeters of clear urine was obtained, followed by 20 cc. of blood. A retention catheter was not thought to be indicated.

Fig. 2 (case 3).—Original roentgenogram made after fixation on a Bradford frame plus a pelvic swathe. Note the upward displacement of the left innominate, and fracture of the left rami and right pubic body.

Fig. 3 (case 3).—Roentgenogram showing the end-result with no residual disability. Note the fusion of the left sacro-iliac with but slight displacement; also the consolidation in front.

The condition of shock resisted most vigorous measures for the first twelve hours. Except after the administration of saline intravenously or after epinephrine, the systolic pressure was between 60 and 75 or was not obtainable. Hypodermoclysis with frequent small doses of caffeine finally seemed most effective and kept the pressure fairly steady around 100 by the end of twelve hours, and at the end of twenty-four hours the quality of the pulse was good, with a pressure of 120 systolic and 80 diastolic.

Roentgen examination showed a severe upward dislocation of the left innominate bone, there being great separation in front in spite of the binder, and in addition a horizontal fracture across the body of the right ilium between the

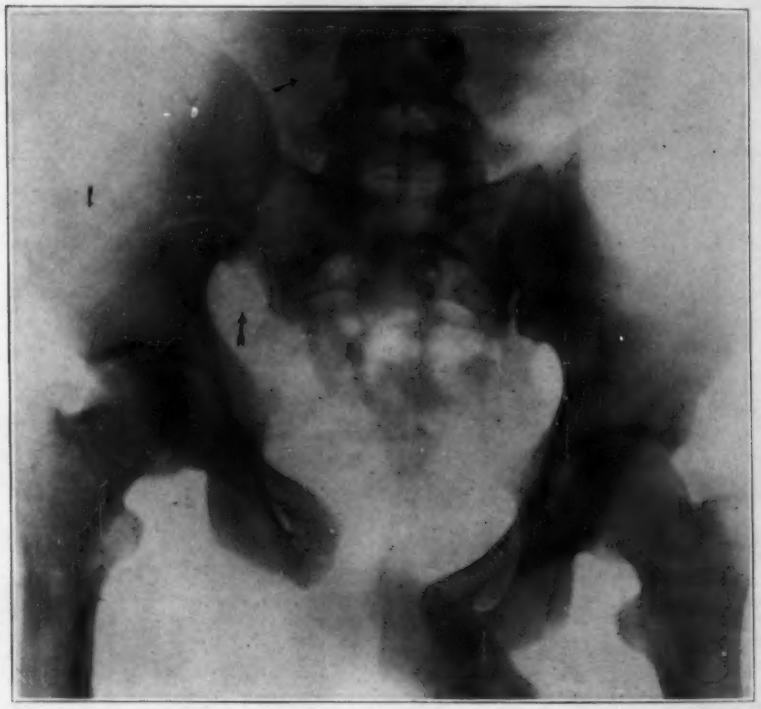

Fig. 4 (case 4).—Roentgenogram showing patient's condition on admission. Slight separation of the left sacro-iliac joint; marked separation and displacement of the right sacro-iliac joint; marked separation and displacement of the symphysis and pubis; upward and outward dislocation of the right innominate bone, 1½ inches at the back and 2 inches at the front and linear fracture across the body of the ilium are noted.

sacrosciatic notch and the anterior superior spine, no displacement, however, being present at the site of fracture.

The patient's condition of shock rapidly changed to one of extreme traumatic psychosis, so that he was either irrational or delirious and required restraint for the first few days. Although the urine became clear after the first day, voiding was not spontaneous until the third day. On the fourth day, tympanites became extreme, and he seemed dangerously toxic, but this condition finally responded to stupes, enemas and a solution of pituitary. During this period the temperature

ranged between 102 and 103 F., and the pulse rate between 120 and 130. On the sixth day, both were slightly lower, and he did not seem at all toxic, though still irrational.

It was then felt that the persisting innominate displacement was a factor in continuing both the organic and the mental disturbances, and reduction under anesthetic was accordingly carried out. The method elsewhere described was again used, and the immediate fluoroscopic control suggested practically complete reposition.

After reduction, improvement in the condition became rapid in every respect. Only one catheterization was required. The patient seemed to have less pain, he

Fig. 5 (case 4).—Pelvis after reduction by closed methods. Upward displacement in the right sacro-iliac is almost completely reduced, but rotation is not completely corrected as evidenced by the level of the pubic bones. There is incomplete reduction of the separation of the symphysis.

was easily managed, and his mental condition became steadily better, though he was not completely cooperative for another week. The traction on the leg and the hammock sling were continued. Bedside films two weeks after reduction, which to clinical examination still seemed complete, showed that there was a rotation or eversion deformity and slight separation persisting at the symphysis. A webbing buckled binder was substituted for the hammock sling, but, though constantly tightened, films after another two weeks showed little change. It was felt that wiring was indicated on this account, but this procedure was deferred until after a cystitis cleared up in the seventh week. Operation was performed on June 23, under ethylene. It was found that even after the bladder and urethra

were freed and the pubic space thoroughly cleared between the two bones, even with maximum contralateral traction on heavy wires passed around each pubic bone, little further apposition could be obtained. The pelvic ring seemed to be solid at the back. The symphysis was wired in the best possible position, and an osteoplastic bridge made across the pubic spines.

Postoperative treatment was by frame and belt. Convalescence was entirely uncomplicated. The patient sat up in bed two weeks after operation and two months after the accident. He was up in a chair a few days later, and on crutches three weeks after operation. At the time of discharge, two days later, he was walking unaided and without limping. There were no shortening and no palpable mobility at the symphysis.

Fig. 6 (case 4).—Roentgenograms showing the end-result four months after wiring; the patient is back at work as a structural iron worker, with no residual disability or complaint. Asymmetry of the pelvis is due partly to the position of the patient, but mostly to an incomplete correction of the rotation deformity. Note the fusion of the sacro-iliac in normal position and the acetabula at the same level. The symphysis pubis is fused by a bony bridge residual from a light graft not clearly shown in the print. An interesting bridging of the lateral process of the fifth lumbar to the right ilium seems to be causing no disability.

The patient was reexamined four months later, about six months after injury, and voluntarily demonstrated his recovery by standing up on a table and jumping down to the floor. His posture showed no list, mobility of the spine was complete, Trendelenberg's sign was negative, and there was no mobility or apparent discomfort on any manipulation of the pelvis. Roentgenograms then obtained and produced here show a bony bridge at the site of the osteoplastic grafts across the symphysis.

CASE 5.—J. P., a mechanic, aged 40, was admitted to the hospital on Dec. 7, 1926, after a crushing blow on the right side of the pelvis. On admission, he was in a rather marked state of shock, with bleeding from the urethra. A retention catheter was inserted, and stimulative treatment in the first twenty-four hours brought considerable improvement. On the second day, symptoms of peritonitis rapidly progressed, and laparotomy was done on the supposition that the bladder was ruptured. At operation, no bladder or other visceral or parietal peritoneal damage was present. There was, however, some free blood-tinged fluid and an extensive rent through a segment of mesentery of the ilium, the vessels of which were thromboid and not bleeding; but the corresponding bowel, for about 18 inches, was deprived of its blood supply and was gangrenous. This loop was brought

Fig. 7 (case 5).—An acute pelvic injury apparently comparable to the preceding illustration but really not containing any true dislocation either front or back, but instead a rather unusual vertical fracture through the sacrum just mesial to the sacro-iliac joint with multiple fractures of the front of the pelvis. Note the great upward displacement of the innominate. The patient was injured by being squeezed and rolled between heavy moving objects. There was a fatal and rather unusual internal abdominal injury, extensive laceration of the mesentery of the small intestine with very little hemorrhage but with progressive thrombosis and intestinal gangrene.

outside of the abdomen for Mikulicz' enterostomy, being opened and drained through both loops twelve hours later. Considerable improvement followed for a few days, when signs of progressive peritonitis again supervened. The patient died on the sixth day after injury. A roentgenogram showed (fig. 7) tremendous upward displacement of one innominate bone.

Case 6.—A. M., a man, aged 54, was admitted to the hospital on Sept. 9, 1927. While walking, he was struck on the side of the body by an automobile, thrown against another car and then to the street. He showed moderate shock for a few hours, with vomiting, but only on taking food or liquids. He could not void spontaneously for the first few hours only; there was no blood grossly or microscopically in the specimens. Diffuse contusions and abrasions were the only injuries ascertained beyond fracture dislocation of the innominate bone. He was removed from the hospital against advice about twelve hours after admission; the result is not known. Figure 8 shows fracture through both rami on the left and dislocation of the sacro-iliac joint with upward displacement of the innominate bone on that side.

Fig. 8 (case 6).—Roentgenogram of injury in a patient who was not treated but was withdrawn from the hospital soon after entry. Note the slight separation of the left sacro-iliac joint with considerable upward displacement of the left innominate bone. A break in the pelvic ring in front occurred through the left pubic bone rather than at the symphysis.

Postmortem examination showed progressive thrombosis of the mesenteric vesseis found injured at operation, with corresponding gangrene of the bowel here, and also thrombosis and gangrene of a remote segment in which no tear or gross evidence of injury appeared.

Case 7.—C. M., a machinist, aged 37, was admitted to the hospital during the morning of Sept. 10, 1927, after being caught in a rolling mill and sustaining a crushing injury to the pelvis. Symptoms of shock were rather moderate at first but increased during the day, symptoms of peritonitis also appearing. Mobility of the pelvis was apparent on admission, and roentgen examination showed a

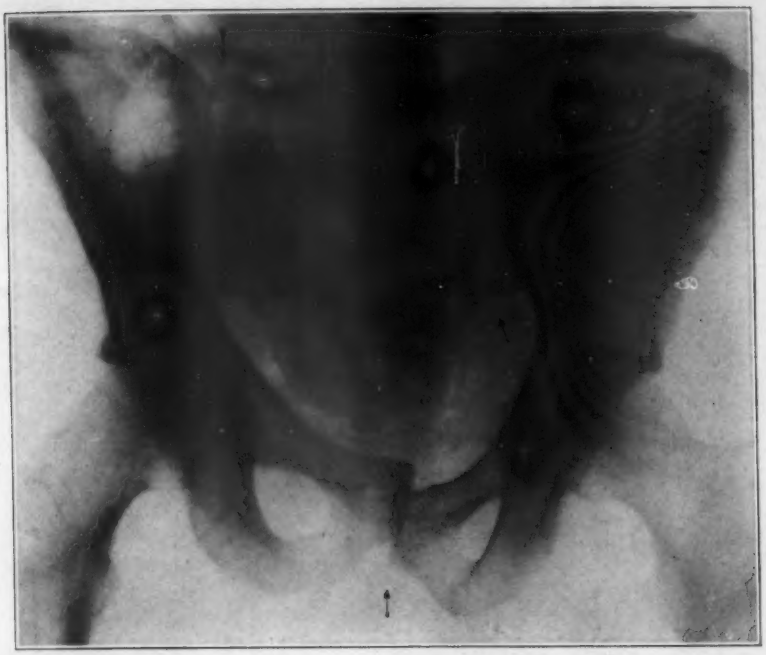

Fig. 9 (case 7).—Condition on admission. Stereoscopic study indicates a fracture dislocation of the right sacro-iliac joint with considerable rotation and some posterior displacement; the overlapping right pubic bone lies posterior to the left. Note separation of the left sacro-iliac joint. This case differs from others in the series in that the displacement of the innominate is backward rather than upward.

Fig. 10 (case 7).—Condition four months after injury; there is no disability referable to injuries of bone. Note the consolidation of both sacro-iliac joints. There has been an osteomyelitis with destruction of the cartilage and some bone of the pubic symphysis which clinically seems solidly held by fibrous tissue.

Fig. 11 (case 8).—Condition on admission. Note fracture dislocation of left sacro-iliac joint, rupture of symphysis pubis and upward displacement of left innominate bone; also fracture in lateral processes of lumbar vertebrae.

Fig. 12 (case 8).—Roentgenogram showing reduction of sacro-iliac fracture and correction of upward displacement of innominate bone secured by simple traction without manipulation. Following examination, a pelvic hammock sling was added, but before illustration was made traction was discontinued to transfer the patient.

luxation of the right innominate bone with an oblique fracture through the ilium running into the sacro-iliac synchondrosis. The innominate bone was displaced slightly posteriorly and at front also mesially, so that the two pubic bones completely overlapped.

As bloody urine was obtained, a diagnosis of injury to the bladder seemed probable; during the day dulness developed in the lower part of the abdomen and also projectile vomiting, leading to laparatomy about eight hours after admission. At operation, laceration of the bladder was found slightly to the left just above the urethra. This was closed, with cystostomy and drainage of the prevesical space. Transfusion was given following operation. The patient improved considerably at first, but a progressive and critical ileus led to enterostomy on the

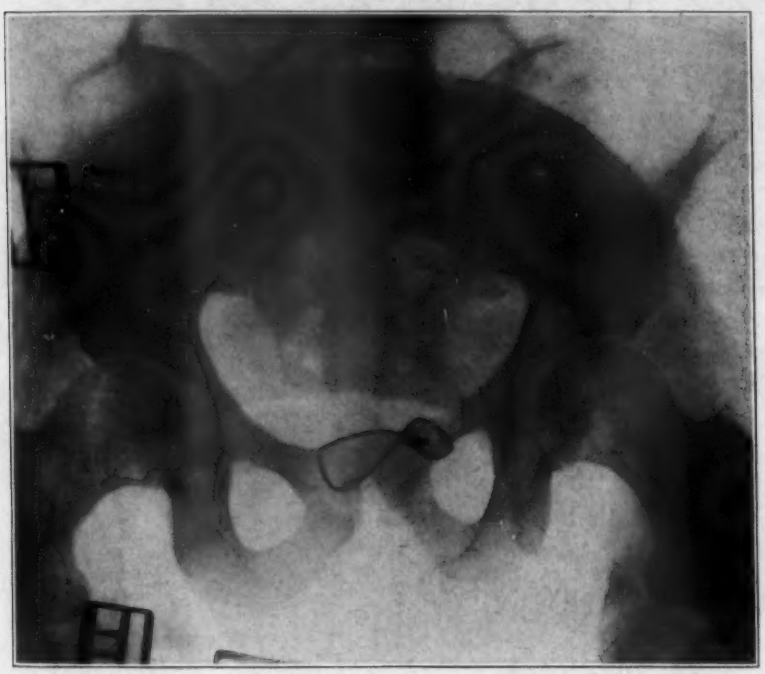

Fig. 13 (case 8).—Usual manipulative technic having failed to correct the recurrence of some upward displacement and rotation of the left innominate, apposition and consolidation of the pubis in front was obtained by wiring with plastic osteotomy of the left pubic bone. Some bony callus can be seen around the lower pole of the left sacro-iliac. This patient was returned to full duty as a machinist.

following day. The distention was gradually overcome, but the patient continued to be quite ill for a long time, with evidence of septic complications. A history of a preceeding chronic cystitis and pyelitis with obviously infected bladder combined with his injuries to make the course a stormy one. Osteomyelitis of the pubic bones developed from the local infection. The fecal fistula was very slow to close. Healing of the suprapubic sinus finally occurred at the end of about four months, and of the fecal fistula about two weeks later.

On account of the injury to the bladder the patient had been transferred to the urological division for operation. Operation verified the roentgen observations as to the position of the pubic bones at the time of cystotomy. No definite manipulative procedures aiming toward reduction were carried out, but the patient was placed on a fracture bed with the body supported on slings; on account of the handling of the indwelling catheter, his legs were left considerably abducted. His condition was such that for many weeks any intervention or manipulation for the skeletal injury was safe. About four weeks after admission, portable films were obtained which showed the relations of the two halves of the pelvis to be normal, save for an increased space at the symphysis pubis. There also was evidence of

Fig. 14 (case 4).—Illustrating technic of closed reduction for innominate displacement. The patient is on a tilting fluoroscopic table hanging suspended by the foot of the displaced side, while counter rotation of the rest of the pelvis is performed by straight leg manipulation on the other side. The assistant steadies the pelvis and verifies the movement of the pubic bones, which is then followed by fluoroscopic check. See details in text.

osteomyelitis of the left pubic bone. Subsequent roentgenograms showed no further change in relations and evidence of healing of the bone infection. Seven months after injury, the pelvis seemed solid on examination and the patient began to sit up, but he did not walk until after another four months. At that time no symptoms referable to skeletal injury prevailed.

Fig. 15 (case 4).—Method of retention of reduction during convalescence by pelvic suspension and longitudinal traction on the displaced side.

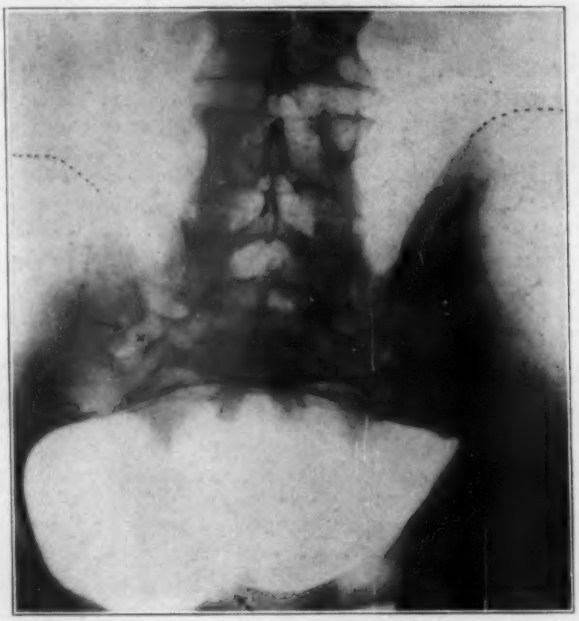

Fig. 16.—Roentgenogram from an old case lately discovered in the files, after the patient was examined for a back complaint. The injury occurred ten years previously with recovery after six months. There was persistent low back pain which spread upward; a clinical diagnosis of ankylosing spondylitis was corroborated by a roentgenogram. See also the difference in the level of the iliac crest and derangement of the symphysis. Roentgenogram taken to show condition of spine.

Case 8.—J. B., a mechanic, aged 26, was admitted to the hospital in the morning of Dec. 8, 1927, a few minutes after an automobile accident in which his car overturned, but the mechanism of the injury was not further recalled. He showed laceration over the right eye, bruises around the trunk and legs, crepitation and severe localized tenderness over the left posterior iliac crest, hypermobility of the pelvis in front, with extreme pain on handling. Roentgenograms showed an upward luxation of the left innominate bone, both pubic and sacro-iliac synchondroses being ruptured, a fracture with slight displacement through the posterior part of the left ilium and fractures of the left lateral processes of the third, fourth and fifth lumbar vertebrae. Roentgenograms of the skull were negative.

The patient was placed on a Bradford frame, and general supportive measures were instituted. During the day he developed rather marked symptoms of shock, which, however, responded to a second intravenous infusion of dextrose. There were also several attacks of vomiting, but only after ingestion. As considerable abdominal tenderness developed, with continued inability to void, catheterization was done, but the urine was clear. During the first few days the patient was at times stuporous or irrational, but no other or further evidence of cerebral injury developed. On the second day, longitudinal traction of 25 pounds on the leg of the displaced side was begun on a fracture bed, but no more vigorous measures of reduction seemed safe in view of his general condition.

At the end of a week, the patient's general condition was very good, but although no wound or external evidence of trauma had been observed, a rather marked parotitis, with considerable elevation of temperature, developed. This responded to conservative measures, but was responsible for further postponement of manipulative treatment of the pelvic displacement. However, roentgen examination made with a portable x-ray apparatus on the thirteenth day, showed apparently complete correction of the upward displacement of the left innominate bone. Traction was therefore discontinued in favor of a pelvic hammock to accomplish reduction of the separation of the symphysis. It was about ten days later that transfer to another building had to be made, and by some oversight, the next examination did not occur until four weeks after admission, when some recurrence of upward displacement with an additional rotation deformity was observed.

Manipulation under the fluoroscope by the technic described was at once carried out, and it was thought that considerable improvement in position was obtained. However, control roentgenograms subsequently showed imperfect apposition with overlapping of the pubic bones in front. Open reduction, with an osteoplasty of the left pubis and wiring, was accordingly performed about six weeks after admission. External fixation after operation was continued in a double plaster spica. Convalescence was uncomplicated, and the roentgenogram showed an apparently satisfactory result. It should be noted that at operation no mobility of the pelvis at the back could be obtained, so that plastic procedure was resorted to to accomplish pubic consolidation. In spite of some persisting rotation of this side of the pelvis, the two acetabula appear at the same level, and there is no clinical shortening of the extremity. The patient has returned to full duty with no complaints.

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CONTRACTURE RESULTING FROM TENOTOMY*

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The term contracture is used to designate prolonged or more or less permanent muscle shortening. The delayed relaxation seen in a nerve-muscle preparation after a series of rapidly repeated contractions, the delayed relaxation caused by veratrine poisoning, the prolonged shortening caused by nicotine and acetylcholine in frog muscle and in denervated mammalian muscle and Tigel's contracture are chiefly of interest to the physiologist. With the exception of the first mentioned, which is generally regarded as a fatigue contracture due to the accumulation of lactic acid in the muscle, not much is known about the physicochemical factors involved in these phenomena. Nor are the structural factors any better understood. The relative parts played by the myofibrils and sarcoplasm are still matters of controversy. In a recent article, Gasser [1] has presented a comprehensive review of the various types of contracture with which the physiologist is familiar and states that these are of an entirely different nature from the myostatic contractures with which this paper deals.

As ordinarily used in clinical literature, contracture designates a condition of persistent tonic shortening of muscles which will, however, relax during sleep or under anesthesia. To this class belong the contractures seen in some patients with lesions of the pyramidal tract. This sort of muscle shortening is maintained by a continuous stream of nerve impulses reaching the muscles from the central nervous system and affecting one group of muscles predominantly or to the complete exclusion of their antagonists. It is, in fact, nothing but an exaggerated and continuous state of hypertonus and is characterized by the deformity which it produces, by its steady persistence during the waking hours, and by the fact that it disappears during deep sleep or anesthesia.[2] Hysterical contracture and the reflex contractures, so often seen during the war, which bear some obscure relation to more or less trifling wounds, also have as their basis an excessive and continuous tonic innervation of the affected muscles. Muscle shortenings of this sort,

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1. Gasser, H. S.: Contractures of Skeletal Muscle, Physiol. Rev. **10**:35, 1930.

2. Oppenheim, H.: Textbook of Nervous Diseases, Edinburgh, O. Schulze & Co., 1911.

whatever their cause, fall in one great group and may properly be designated as hypertonic contractures.

Apparently even in contractures of pyramidal origin there may develop some intrinsic shortening in the muscles, for according to Foerster,[3] while these contractures are due in large part to hypertonus, they are also in part due to the fact that each muscle group adapts itself to the approximating of its points of insertion by the gradual development of contraction and permanently retains this condition of shortening. If this actually occurs, the affected muscles should not fully relax under an anesthetic, and the residual shortening that persisted under deep anesthesia would belong in the class to be described next.

Under the general heading of myostatic contractures have been included a group quite different from the preceding (Ranson and Sams [4]). It includes all contractures that are caused by the fixation of the muscle at a given length for a considerable period of time. Familiar examples are the contractures that restrict the movements of joints after immobilization for weeks in plaster casts, the permanent shortening of muscles after division of their tendons, and probably, in their early stages at least, the paralytic contractures due to the unequal paralysis of antagonistic muscle groups in anterior poliomyelitis and multiple neuritis. Since they all are caused by fixation of the muscle for a long time at one unchanging length, this group of contractures might not improperly be designated as immobilization contractures, but the term myostatic more accurately describes the condition.

By myostatic contracture we mean to designate a condition of permanent shortening in resting muscle which is maintained in the entire absence of nerve impulses, the muscle having acquired, usually as a result of prolonged immobility, a new and shorter resting length. It is the condition which has been designated "Ruheversteifung" by Spiegel and Shiboya.[5] These investigators and others as far back as 1886 (Moll [6]) have clearly demonstrated that if the bony attachments of a skeletal muscle are immobilized for several days so as to prevent the changes in length that normally result from spontaneous and reflex movements, there occurs a fixation of the muscle at the

3. Foerster, O.: Die Kontrakturen bei den Erkrankungen der Pyramidenbahn, Berlin, S. Karger, 1906.

4. Ranson, S. W., and Sams, C. F.: A Study of Muscle in Contracture: The Permanent Shortening of Muscles Caused by Tenotomy and Tetanus Toxin, J. Neurol. & Psychopath. **8**:304, 1928.

5. Spiegel, E. A., and Shiboya, H.: Die Bedeutung des Zentralnervensystems für die Entstehung muskulärer Contracturen an eingegipsten Extremitäten, Ztschr. f. d. ges. Exper. Med. **44**:729, 1925.

6. Moll, A.: Experimentelle Untersuchungen über den anatomischen Zustand der Gelenke bei andauernder Immobilization derselben, Virchows Arch. f. path. Anat. **105**:466, 1886.

length thus imposed on it. If taken sufficiently early, this contracture can be overcome by active or passive movements, but if it is left untreated for some time the damage becomes irreparable.

It may be that adhesions and ankylosis play a part in the limitation of motion in a joint that has been enclosed for weeks in a plaster cast, but these factors are certainly secondary to the shortening of the muscles. This is clearly shown by the following experiment (Moll [6]). After the hind leg of a rabbit had been enclosed in a plaster cast for twelve days, division of the muscles completely eliminated all of the resistance to passive movement which had developed. This showed that within this time no adhesions, thickenings of the joint capsule or changes in the articular surfaces had developed and that the limitation of movement was entirely due to a shortening and fixation of the muscles.

Fröhlich and Meyer [7] have shown that this fixation of an immobilized muscle is dependent on the nerve impulses that reach it from the central nervous system. Immobilization of a denervated muscle does not cause it to become set or alter its extensibility as would be the case if the nerve supply were intact. According to these authors, section of the dorsal roots supplying the muscle is sufficient to prevent the contracture, indicating that the integrity of the local reflex arc is essential for its development.

Spiegel and Shiboya [5] removed the left motor cortex from cats and found that in the right hind leg the extensor muscles became set more quickly than the flexors, while flexor rigidity was more easily induced on the left side. They carried out other experiments, transecting the spinal cord in the lower thoracic region and then putting the limbs up in plaster casts in the flexed position, and found that setting occurred in the fore limb more quickly than in the hind limb. These experiments indicate that the brain centers that control tonic innervation of the muscles play an important part in the genesis of this phenomenon.

Myostatic contracture is then the fixation or setting of an immobilized muscle in a new and shorter than normal resting length. In its genesis it is dependent on the nervous system and it is probably an abnormal manifestation of tonic innervation. It is, however, only in its genesis that myostatic contracture is dependent on the nervous system. After it has once developed, it is independent of the innervation and persists under deep anesthesia and even after section of the motor nerve. It is a contracture of muscle at rest and is in this respect to be sharply distinguished from the hypertonic contractures previously mentioned.

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7. Fröhlich, A., and Meyer, H. H.: Untersuchungen über den Tetanus, Arch. exper. Path. u. Pharmakol. **79**:55, 1916.

Many of the attempts at explanation of contractures of various types have dealt with the hypertonic forms, and a number of the papers have been for the most part reviews of the literature on the controversial questions of muscle tonus. The papers of Buscaino,[8] Cooper,[9] Crocq,[10] Noica,[11] Pieron,[12] and Ott [13] contribute nothing of importance to the problem. Probably the most significant single observation is that attributed by Oppenheim [2] to Brissaud, namely, that an anemia of the affected extremity produced by an Esmarch bandage has a relaxing effect on the shortened muscles. It suggests that the shortened state is not maintained by structural alterations in the muscle, but by a chemicophysical equilibrium that is upset by the anemia.

Ranson and Sams' [4] study of myostatic contractures produced by tetanus toxin and by section of the tendo achillis in rats and cats dealt with the capacity for shortening that the gastrocnemii of these animals retained in their shortened state and the speed of relaxation from nerve-muscle tetanus.

Kymograph records showed that a muscle in myostatic contracture cannot shorten so much as a normal muscle during nerve-muscle tetanus. In these experiments the average normal shortening of the rat's gastrocnemius during contraction was found to be 7.5 mm., and this was reduced to an average of 4.6 mm. for the muscles in contracture. While the capacity for shortening during nerve-muscle tetanus was decreased to the same extent in both types of experimental myostatic contracture, the rate of relaxation was unaffected by tenotomy but was considerably reduced by tetanus toxin.

The height of contraction and the rate of relaxation of a muscle in tetanus contracture were the same whether the muscle was stimulated directly or through its nerve. This showed that the defective contraction cannot be explained on the basis of an involvement of the nerve or nerve endings.

Changes in length of the muscles and of individual fibers, and changes in weight were also noted. In both tetanus contracture and that following tenotomy, fibers in the cat's and rat's gastrocnemius had

8. Buscaino, V. M.: Genesi tossica della contrattura; esperimenti e critiche, Riv. di. pat. nerv. **17**:330, 1912.

9. Cooper, G.: Contractures and Allied Conditions, Brit. M. J. **1**:109, 1917.

10. Crocq. J.: Le mécanisme du tonus musculaire des reflexes et de la contracture, Encephale **9**:147 and 197, 1914.

11. Noica, M.: Le mécanisme de la contracture spasmodique, Presse méd. **19**: 153, 1911.

12. Pieron, H.: Du mécanisme physiologique du tonus musculaire comme introduction a la théorie des contractures, Presse méd. **26**:88, 1918.

13. Ott, A.: Considerazioni sulla fisiopatologia della contrattura, Riv. di pat. nerv. **17**:429, 1913.

become permanently shortened 45 or 50 per cent of their normal length, but owing to the obliquity of the fibers the muscle as a whole underwent a shortening of only 10 or 12 per cent. The weight of the muscle remained normal in tetanus contracture, but after tenotomy there was an average loss of weight of 18 per cent.

Davenport, Davenport and Ranson [14] have found that the lactic acid content of rabbit and guinea-pig muscles in the contracture caused by tetanus toxin is within the same range as that of normal muscles either from the unaffected side of the same animal or from normal animals. The glycogen content [15] of guinea-pig and rabbit gastrocnemii is usually reduced during the early stages of the contracture while it is still dependent on innervation. Rats show little change in glycogen content at the same period. In later stages of tetanus contracture the glycogen content of contracted and normal sides is usually about the same, though frequently both are lower than in normal animals. The glycogen content seems to bear no causative relationship to contracture. Wertheimer's [16] experiments led him to believe likewise that glycogen change had little to do with contracture. Determinations of changes in acid-soluble phosphorus fractions in rabbit muscles in tetanus contracture [17] showed an apparent reduction in the total quantity and a similar decrease in phosphocreatine. Determination of protein nitrogen in these muscles indicated that the water content of the muscle in tetanus contracture was greater than that of the normal. The decrease in total phosphorus was proportional to the increase in water in the muscle and the decrease in phosphocreatine was only a little greater than could be accounted for by the change in water content. Since tetanus muscles are more irritable than normal ones, stimulation occurring during freezing may have been responsible for the reduction of phosphocreatine. It is believed that there was no significant change in absolute quantities of acid-soluble phosphorus fractions, since the remaining fractions varied inconstantly. The fat content in tetanus muscles of rabbits was 10 per cent greater in three of five animals, and in the other two it was the same as the normal muscles.

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14. Davenport, H. A.; Davenport, H. K., and Ranson, S. W.: Chemical Studies of Muscle Contracture: I. The Lactic Acid Content, J. Biol. Chem. **79**:499, 1928.

15. Davenport, H. A.; Davenport, H. K., and Ranson, S. W.: Chemical Studies of Muscle Contracture: III. The Change in Glycogen During Shortening Produced by Tetanus Toxin, J. Biol. Chem. **82**:499, 1929.

16. Wertheimer, E.: Verändert sich der Glykogenbestand bei der tonischen Contractur quergestreiften Muskeln, Arch. f. d. ges. Physiol. **221**:139, 1929.

17. Davenport, H. A.; Davenport, H. K., and Ranson, S. W.: Chemical Studies of Muscle Contracture: IV. Changes in Phosphorus, Nitrogen, and Fat Content During Shortening Produced by Tetanus Toxin, J. Biol. Chem. **87**:295, 1930.

Experimental work on changes in structure of skeletal muscle in various stages of contraction and kinds of contracture has been done by Frank.[18]. He determined by measurement of the cross-striations, the relationships between the widths of isotropic and anisotropic bands in isometric contraction, stretched isometric contraction, stretched resting muscle, fatigue contracture, chloroform contracture and rigor mortis. He found the ratio of the width of isotropic to anisotropic bands the same in chloroform contracture, rigor mortis, resting muscle and in complete fatigue. This was different, however, from the ratio found in varying degrees of contraction. He believed, therefore, that true contractions and contractures of various kinds are not of the same nature.

Hürthle's [19] recent experiments on frog muscle were undertaken because Frank's work on frog muscle disagreed with work which Hürthle had done on *Hydrophilus* muscle. Hürthle investigated the effects of chemical fixation on the maintenance of contraction produced by electrical stimulation. His use of kymograph tracings made during fixation of the muscle while it was being stimulated, showed some differences in response to various fixatives and a partial relaxation of the muscle from the initial contraction induced by the fixative, which Frank believed augmented that caused by electrical stimulation. He was able to obtain the same histologic picture that Frank did when his material was handled in the same way, but in view of the variation caused by different methods of handling, he did not feel that such a picture could be taken as the true condition of living muscle.

Nageotte [20] studied the microscopic changes in frog muscles in the extreme contracture produced by faradic stimulation and that produced by exposure to strong chloroform vapors.[21] He obtained fibers presenting under the microscope a mottled appearance, which he interpreted as contraction of the myofibrils in spots since it could be prevented if the muscle were pulled out slightly before fixation. The early stages of chloroform contracture resembled various stages of faradic contraction and were also reversible so long as the muscle remained elec-

18. Frank, G.: Das histologische Bild der Muskelkontraktion, Arch. f. d. ges. Physiol. **218**:37, 1927.

19. Hürthle, K.: Zur Kenntnis der Struktur des ruhenden und des tätigen Froschmuskels: I. Abhandlung. Lässt sich die Struktur des Froschmuskels im Zustand der Verkürzung durch chemische Fixierungsmittel festhalten? Arch. f. d. ges. Physiol. **223**:685, 1930.

20. Nageotte, J.: Sur la contraction extrême du muscle strié chez la grenouille, Compt. rend. Acad. d. sc. **180**:761, 1925.

21. Nageotte, J.: Sur la morphologie du muscle strié en état de contracture chloroformique chez la grenouille, Compt. rend. Acad. d. sc. **180**:1963, 1925.

trically excitable, but in the later irreversible stage when plasma was expelled from the fibers and coagulated on the surface the picture was quite different.

Gavrilescu [22] has repeated Nageotte's work on chloroform contracture studying fixed and stained material and, in addition, the fresh, unstained fibers. He confirmed Nageotte's work on the stained material. In the fresh material, however, contraction waves could be seen moving down the fibers when they were exposed to chloroform. The cross-striations were altered in the contracted portion of the fiber as the wave passed along, the dark bands appearing to approach closer to one another so that the contracted part was darkened. The author was unable to say whether there was a reversal of striation. In order to eliminate the chemical factor that might possibly be involved in chloroform contracture, he [23] carried out another series using direct electrical stimulation. Here also he examined both stained and fresh muscle. His observations agreed with those of Nageotte for stimulated muscle on the stained tissue, but in fresh muscle stimulated to contracture and then examined in physiologic solution of sodium chloride, there was no alteration in striation and the fibers appeared normal.

In a note concerning Gavrilescu's work, Nageotte [24] refers to his own work [20] in which he had observed a tendency for the muscles to relax a little spontaneously after cessation of stimulation and in which it was possible to stretch them out to normal length with a little gentle traction. He does not, therefore, believe it possible to dissect off small pieces of fresh muscle from the contracted muscle and maintain extreme contracture.

The microscopic changes occurring in rat's gastrocnemii in contracture produced by tetanus toxin have been studied in this laboratory.[25] The fibers showed more pronounced longitudinal fibrillation and blurred cross-striations. The blurring of the cross-striations was due in part to a loss of alinement of myofibrils and in part to lack of uniformity in reaction to stains in different parts of the fibers. This produced a mottled effect which will be described in more detail later in the paper. Measurements of the width of isotropic and anisotropic bands in regions

22. Gavrilescu, N.: La contracture chloroformique et les modifications de la fibre strieé, Compt. rend. Soc. de biol. **101**:771, 1929.

23. Gavrilescu, N.: L'aspect de la fibre musculaire strieé lors de la contracture éléctrique, Compt. rend. Soc. de biol. **101**:852, 1929.

24. Nageotte, J.: Au sujet de l'aspect histologique de la fibre musculaire strieé lors de la contracture éléctrique, Compt. rend. Soc. de biol. **101**:990, 1929.

25. Davenport, Helen K.; Ranson, S. W., and Stevens, E.: Microscopic Changes of Muscle in Myostatic Contracture Caused by Tetanus Toxin, Arch. Path. **7**:978 (June) 1929.

taking the stain with different intensity showed that their spacings bore no relation to the intensity with which a given part of a fiber stained, so that the darker color was not due to widening or approximation of anisotropic bands in one region and reversal of the condition or normal spacing in another. Some fibers stained uniformly, but the isotropic bands were narrowed throughout. There was frequently great variation between the appearance of adjacent fibers in the same field. Scattered fibers in some specimens appeared to be undergoing degeneration. There was some increase in sarcolemma nuclei and in the number of large wandering cells. Cross-sections showed an increase in the thickness of the fibers, and measurements showed that they were 23 per cent greater in diameter than the normal fibers. No increase in connective tissue could be seen. Figures for the total shortening of the muscle and for the shortening of individual fibers were found to be about the same as those given by Ranson and Sams for muscle in tetanus contracture. Likewise, there was no decrease in weight in the tetanus muscles. The changes observed did not explain the fixation of the muscle in the shortened state.

The present paper deals with the microscopic changes that take place in the gastrocnemius muscle of white rats, guinea-pigs and cats in which the tendo achillis has been sectioned and makes a comparison of such changes with those already outlined for tetanus contracture.

METHOD

Four cats were killed seventeen days, two guinea-pigs and ten rats sixteen days, and three rats forty-four days after section of the tendo achillis in the right leg. The left gastrocnemius served as control. The gastrocnemii were dissected out immediately on the death of the animal. Before removal of the right gastrocnemius from the leg, the distance between the cut ends of the tendon was measured while the ankle was held at a right angle. This was done only on rats. The muscles were then removed and suspended in a moist chamber for one hour under a tension of 50 Gm. for rats, 100 Gm. for guinea-pigs and 200 Gm. for cats, and then placed in fixing fluid with the weight still attached. Fixation and staining methods were the same as those employed in the study of muscle in tetanus contracture, i.e., formaldehyde U.S.P. (1:10), Zenker's fluid and Bouin's fluid for fixation; and for staining, hematoxylin and eosin, iron hematoxylin, van Gieson's picrofuchsin, and Mallory's triple connective tissue stain. All four stains were used after each fixative since the manner of fixation permitted the use of only one fixative on a given animal.

After fixation, the right and left gastrocnemii of each rat were dried off carefully with filter paper and weighed and measured. The total length of the muscle and the length of the fibers in an easily identifiable bundle were measured in both the shortened and control muscles.

Paraffin sections, longitudinal and transverse, from 6 to 8 microns thick, were prepared for microscopic study. Sections from both the control and the shortened muscle were mounted on the same slide to insure uniformity of treatment.

RESULTS

Gross Changes.—The gastrocnemii of which the achilles tendon had been cut showed the typical picture of contracture. They were short and plump and had pulled the cut ends of the tendon apart. The distance between the cut ends, as measured while the ankle was held at a right angle, varied from 6.5 to 12.8 mm. in rats. The three rats that had been kept for forty-four days after tendon section showed fairly well defined new tendons formed by a filling in of the space between the cut ends of the old one, presumably with connective tissue, though no histologic examination was made of the tissue. Two of these animals had regained the function of their limbs so that there was little difference in the way they used their hind legs. The third rat had regained considerable function also, but it was not so nearly normal as the other two. The space between the cut ends of the old tendon was greater in this rat than in the others.

Some atrophy had taken place in our preparations in which the tendon had been sectioned. This was shown by the difference in the weights of the right and left gastrocnemii. The average weight of the shortened muscles of rats was 0.91 Gm., that of the normal muscles, 1.14 Gm. The loss of weight averaged 20 per cent. The shortened muscles of two cats averaged 15.8 Gm., the normal 20 Gm., showing a loss of 21 per cent in weight. The muscles of two of the cats and the guinea-pigs were not weighed or measured but presented the same short, plump appearance as those which were. Audova [26] found in his experiments on rabbits in which the tendo achillis had been cut for from twelve to sixteen days that there was an average loss of weight in the fresh muscle of 19.1 per cent. Lange [27] did some experimental work on rabbits to determine the importance of tension for muscle atrophy and regeneration. He cut the achilles tendon and excised a piece of it together with from one third to one half of the gastrocnemius. In one series of experiments a silk thread was attached to the remaining stump of the gastrocnemius at one end and the calcaneus at the other and drawn as tight as possible without pulling it out of the muscle. Regeneration did not occur after four months. Degeneration was present instead. In another series the thread was adjusted to approximate the normal tension. Here regeneration started from the muscle down over the thread in about eight weeks, and after sixteen weeks the preparation had the appearance of normal muscle with normal tendon. In a third series, a connection was made between

26. Audova, A.: Ueber den zeitlichen Verlauf der Muskelatrophie nach Sehnendurchschneidung, Schweiz. Arch. f. Neurol. u. Psychiat. **10**:211, 1922.

27. Lange, M.: Die Bedeutung der Spannung für die Muskelatrophie und Muskelregeneration, Verhandl. d. deutsch. orthop. Gesellsch. **23**:230, 1929.

muscle and calcaneus with silk thread, but the thread was left with no tension at all. Here atrophy occurred until the gastrocnemius had nearly disappeared. No histologic study was made of these muscles. This bears out the observations of Meyer [28] that atrophy occurs in relaxed muscles.

The amount of shortening of the muscle and of individual fibers in the series of rat muscles is shown by the following figures. The total length of the normal muscles averaged 30.4 mm. and of the shortened muscles, 26.3 mm., which is a shortening of 13 per cent. The minimum shortening was six per cent, the maximum 22 per cent. The individual fibers measured in the normal gastrocnemii averaged 10.1 mm. in length, and in the shortened ones, 6.8 mm. This was a decrease of 32 per cent in length. These figures are similar to those found for tetanus muscle. The oblique course of the fibers through the muscle would account in part for the discrepancy between the amount which the whole muscle was shortened and that which the individual fibers shortened.

Microscopic Changes.—After tenotomy, as in tetanus contracture, the greatest alteration occurred in the arrangement and the staining properties of the myofibrils. Longitudinal striation was more pronounced and cross-striation blurred. The blurring of the cross-striation came about in different ways, for the histologic picture was not a uniform one, since adjacent fibers in a specimen frequently had quite different appearances. This is well illustrated in figure 2. Some fibers or portions of fibers were thrown into a wavy contour and the fibrils therefore twisted so that when cut in longitudinal section, one could see cut ends of fibrils alternating with regions of distorted cross-striations running obliquely across the fiber in one direction or another according to the direction of the fibrils at that place (fig. 2, *d* and *e*). Under low power magnification, these fibers were striped across with light and dark. This, however, is quite different from the light and dark mottled staining found in other fibers and illustrated in figure 2, fiber *a*, and figures 3 and 4. The mottled staining referred to here is similar to that seen in tetanus contracture. It seemed to be due in part to a loss of affinity for stain in some portions of a fiber, while adjacent areas in the same fiber stained normally or darker than normal, showing a gradation into the nonstaining or lightly staining areas. The configuration of these areas was very irregular, sometimes taking the form of fairly wide zigzag bands across the fiber, sometimes interlacing to give a lattice-like effect as seen in figure 3. The lattice-like appearance was intensified by the separation of the fibrils which produced

28. Meyer, A. W.: Theorie der Muskelatrophie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **35**:651, 1922.

the longitudinal fibrillation. Figure 4, which is a higher magnification of fibers *a*, *b* and *c* of figure 3, shows this very well. In a number of fibers, regions were seen in which the same group of isotropic and anisotropic bands could readily be traced across normally or darkly staining and lightly or nonstaining areas. In some regions they maintained their normal spacings; in others, the *J* band was narrowed. As was the case in tetanus contracture, no definite relation could be seen between the dark and light staining regions of the fiber and the regions in which the stripes were normal or narrowed. Both narrowed and normal spacings were found in both light and dark regions, as can be seen in figure 4. The mottling could not, therefore, be attributed to contraction of the fiber in spots. The possibility that this effect might be due to poor differentiation was eliminated by checking the iron hematoxylin sections with others stained by picrofuchsin, hematoxylin and eosin and Mallory's triple stain, all of which showed mottling of the same regions. Neither could fixation be responsible, since mottling occurred after all of the three fixatives used. In tetanus there were, in addition to normally staining and lightly staining areas in fibers, regions that stained very darkly and in which the striations were obscured except at the edges, where a dark field joined a light one. Here also one occasionally found lightly stained stretched areas between the very dark ones. Such extreme contrasts were not seen in the contracture from tenotomy.

Besides mottled fibers, there were others that stained very lightly throughout, with cross-striations barely visible. Still other fibers illustrated in figure 2, *b* and *c*, had blurred cross-striations resulting from a loss of alinement of myofibrils so that the *J* bands and the *Q* bands in adjacent fibrils did not lie in line and the striations did not therefore appear continuous all the way across the fiber, as is the case in the normal fibers shown in figure 1. The loss of alinement seemed to be due to rupture of the interfibrillar portions of those membranes (*Z* membranes) that bind the myofibrils together. Small groups of fibrils or individual fibrils became separated from their fellows and were displaced slightly in a longitudinal direction, breaking up the continuity of cross-striation.

In some muscles, all of the aforementioned changes could be found side by side. Other muscles showed only one or two of the changes. Six of the seventeen animals studied failed to show mottled fibers. This included the three that had regained function through growth of connective tissue between the cut ends of their tendons. The presence or absence of mottled staining was not dependent on the degree of shortening, however, for two rat muscles showing it very well had shortened 19 and 13 per cent, while another that had shortened 22 per cent had none at all. The three rats which had had their tendons cut

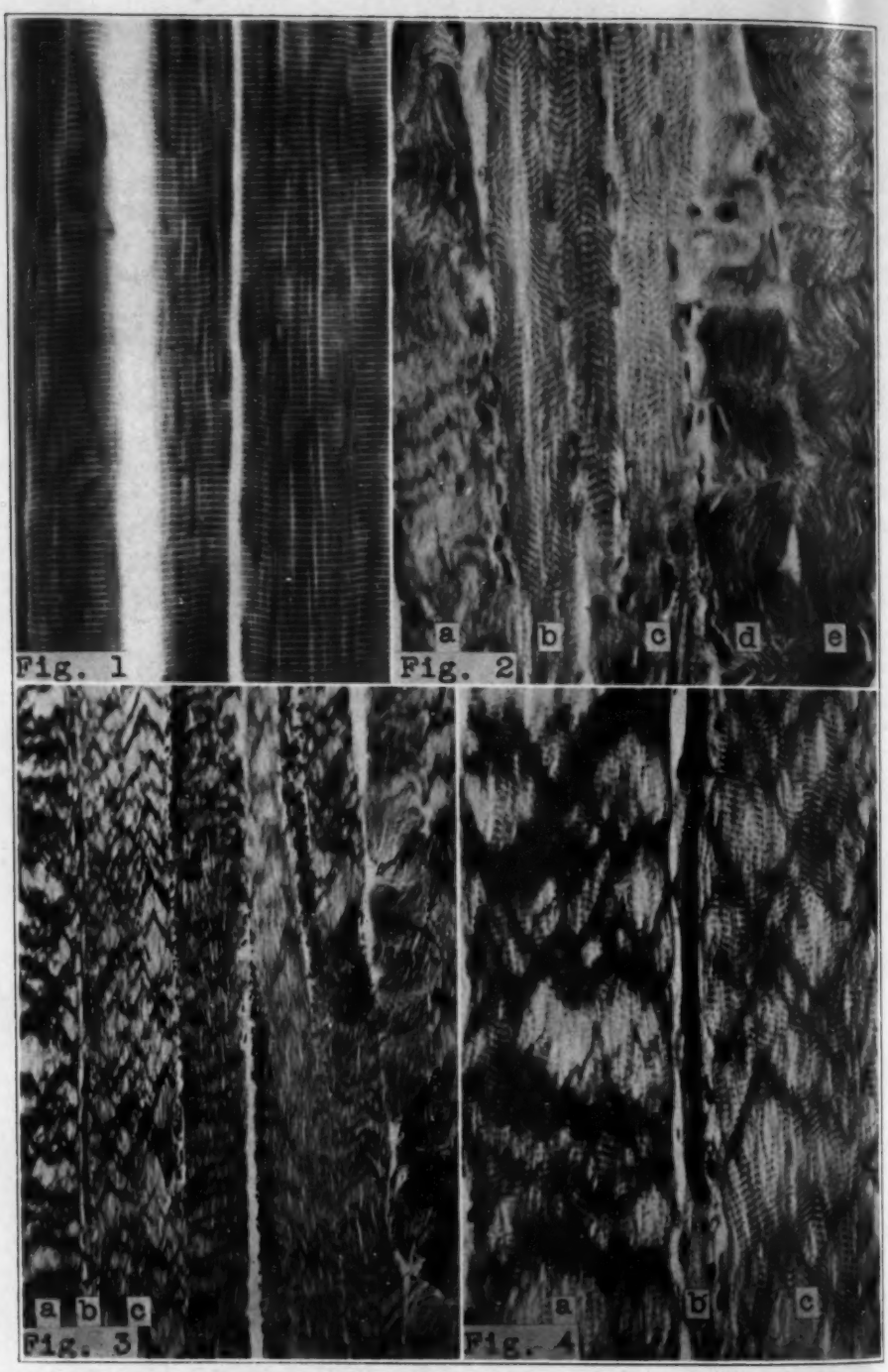

Fig. 1.—Longitudinal section of normal gastrocnemius (rat). Iron hematoxylin; × 395.

Fig. 2.—Longitudinal section of gastrocnemius (rat) sixteen days after section of tendo achillis: (*a*) blurred striations, mottled staining; (*b*) and (*c*), loss of alinement in myofibrils; (*d*) and (*e*) wavy fibers. Iron hematoxylin; × 395.

Fig. 3.—Longitudinal section of gastrocnemius (cat 1) seventeen days after section of tendo achillis, showing mottled staining, longitudinal fibrillation. Iron hematoxylin; × 110.

Fig. 4.—Higher magnification of figure 3, fibers *a*, *b* and *c*; × 395. *a* and *c* show lattice effect in staining; (*b*), very small fiber, thought to be a red fiber squeezed between two pale fibers.

for forty-four days had muscles that were 6, 13 and 19 per cent shorter than the normal, and none of them had mottled fibers.

The thickening of the fibers resulting from their shortening was apparent in longitudinal as well as in transverse sections. The difference in size of the fibers of normal muscle and muscle in contracture is illustrated by figures 5 and 6. Figure 5 is from the gastrocnemius in contracture, and figure 6 from the normal gastrocnemius of rat 8. The areas photographed were taken from approximately the same regions of the two gastrocnemii. The muscles in contracture always stained more lightly and looked less dense than the normal ones. In both longitudinal and transverse sections, the myofibrils seemed not to be packed so close together as in normal muscle. This coupled with a decreased affinity of parts of the fibrils themselves for the stain would account for the lighter histologic picture.

Clearly defined vacuoles were present in scattered fibers in only half of the animals studied. Vacuolation here differed from that seen in tetanus in number and distribution of vacuoles. Here they usually occurred singly as seen in cross-section, and rarely were nuclei seen near a vacuole within the fiber, whereas in tetanus, several vacuoles with nuclei at their edges were often seen in one fiber.

Degenerative changes such as were seen in tetanus did not appear in these experiments. There were no fibers in which the contractile substance had been replaced by nuclei and none in which it had degenerated to a homogeneous mass. Nuclei deeply situated within the fibers were seen in both normal and contracted muscle, in some cases in greater numbers on the side of contracture, in others, more on the normal side. Since the gastrocnemius is a mixed muscle, the red fibers could account for the appearance of nuclei in this position. In a very few fibers observed in the shortened muscle, a small group of fragmented or shrunken nuclei was seen deeply situated. These nuclei may have invaded the fibers from outside or they may have been degenerating muscle nuclei for they stained more darkly than normal muscle nuclei. This, however, occurred in a very small number of fibers and was even seen once in normal muscle, so it seems to have little significance.

There was not a marked increase in muscle nuclei. Some specimens showed no increase; others showed a slight increase with loss of orderly arrangement where the fibrils were twisted. Occasional groups of two or three large rounded nuclei overlapping one another were found in both shortened and normal muscle, but more frequently on the side of contracture. In some instances these appeared to be situated in the fiber, but since the same type of rounded, lightly staining nuclei were also seen outside of fibers and frequently associated with capillaries running across fibers, but readily distinguishable from endothelial nuclei, it is thought that they may have been the nuclei of connective tissue wandering cells. Distortion of the fibers may have caused these

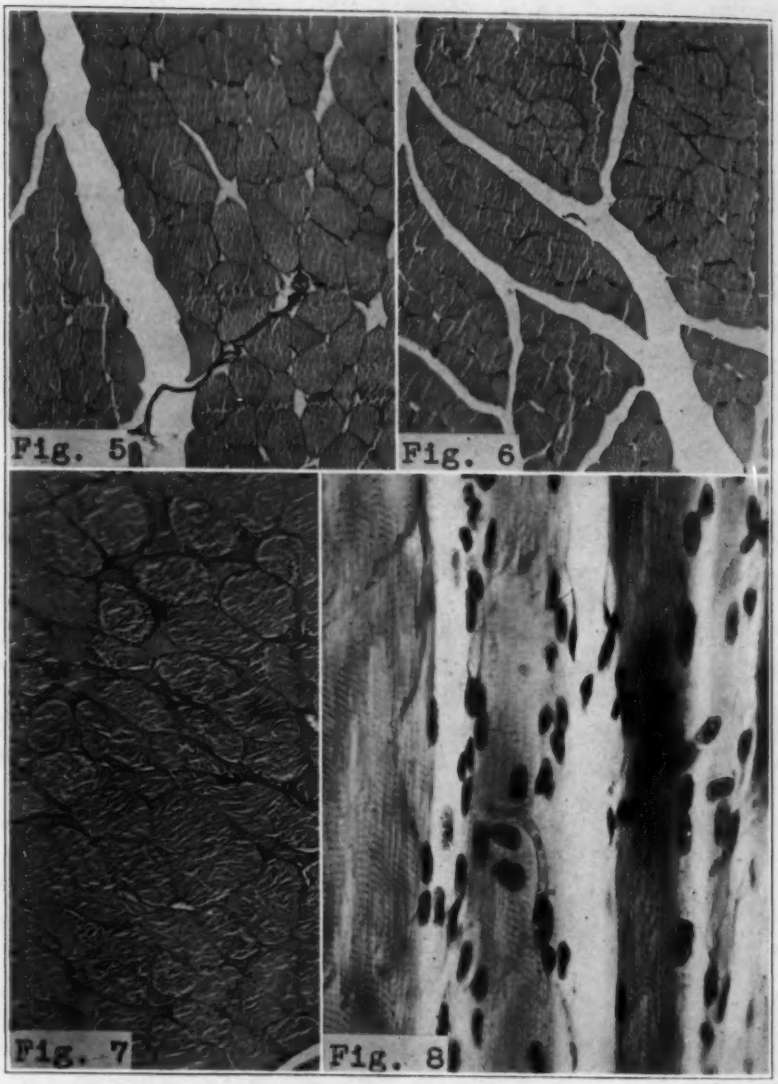

Fig. 5.—Transverse section of gastrocnemius of rat 8 sixteen days after section of tendo achillis. Van Gieson stain; × 110.

Fig. 6.—Transverse section of normal gastrocnemius of rat 8, taken from the region corresponding to that shown in figure 5. Van Gieson stain; × 110.

Fig. 7.—Transverse section of gastrocnemius of cat 2, seventeen days after section of tendo achillis, showing flattened and more darkly stained red fibers between the larger more rounded pale fibers. Van Gieson stain; × 110.

Fig. 8.—Longitudinal section of gastrocnemius of cat 1 showing type of nuclei in vicinity of blood vessel, that were increased in numbers in the shortened muscles. Hematoxylin and eosin; × 450.

nuclei to appear as though they were embedded in the fiber. Three of this type of nuclei are illustrated in figure 8. Two of them appear below the branched capillary in the center of the field and one above it. Of the two below the capillary, the lowermost one focuses in a higher plane than the one nearest the capillary. A third elongated nucleus not in focus and just to the left of the two mentioned is more deeply situated and seems to be a muscle nucleus. Endothelial nuclei are seen in both the upper and lower branches of the capillary. In two of the cats there was an increase in the typical elongated muscle nuclei and an increase in the nuclei of connective tissue wandering cell type in the region of capillaries. Most of the rats showed only an increase in this latter type of nuclei without any discernible difference in number of muscle nuclei. A few short chains containing from three to eleven muscle nuclei were present in both normal and contracted muscle. They were no more numerous in the contracted muscle than in the normal, and therefore cannot be considered characteristic of contracture or essentially pathologic as they are in myotonia atrophica, where there are many chains and the nuclei in individual chains may number forty or more (Heidenhain,[29] Weil and Keschner,[30]).

An increase in connective tissue between fascicles or between fibers was difficult to determine by differential staining with van Gieson's picrofuchsin, or with Mallory's triple stain. Comparison of cross-sectional areas from the same parts of contracted and control muscles in rats showed no more connective tissue on the side of contracture than on the normal (figures 5 and 6). The connective tissue in the specimens of cat and guinea-pig muscle differed in appearance on the two sides. In the shortened muscle it stained deep pink with acid fuchsin, while in the normal it was red. The thin bands of connective tissue separating the fibers of the shortened muscle seemed a little broader and less dense than the normal, in which they formed a very sharp outline for the fibers. It seems possible that a change may have taken place in the character of the connective tissue without an actual increase in quantity. Another observation that would point to either an increase in quantity or in tensile strength in the connective tissue was the difference between the behavior of the shortened muscle and the normal during the processes of preparation for staining. When frozen sections were made for fat staining, both longitudinal and cross-sections of the muscles in contracture held together throughout the process of staining and mounting, whereas the normal ones tore apart very easily, and the separation occurred between the fibers. In paraffin embedded blocks taken from

29. Heidenhain, M.: Ueber progressive Veränderungen der Muskulatur bei Myotonia atrophica, Beitr. z. path. Anat. u. z. allg. Path. **64**:198, 1918.

30. Weil, A., and Keschner, M.: Ein Beitrag zur Klinik und Pathologie der Dystrophia myotonica, Ztschr. f. d. ges. Neurol. u. Psychiat. **108**:687, 1927.

the same gastrocnemii as the blocks for frozen sections, shortened muscles cut more easily and did not have a tendency to shatter like the normal ones. Both shortened and control muscles received exactly the same treatment throughout fixation, embedding and staining.

The difference in cutting of the paraffin sections might also be due to changes in the muscle fibers which would prevent the shortened muscles from hardening so much in dehydration and embedding as the normal ones. A comparison of the relative amounts of water in shortened and normal muscles was not made in this series of experiments. Lipschutz and Audova [31] and Audova [26] found that the relative amount of water in the rabbit's gastrocnemius was greater after the achilles tendon had been cut or after nerve section than in normal muscle.

The atrophy which was indicated by loss of weight was not apparent microscopically unless the lighter staining centers of some fibers near the tendon be considered early atrophy, though they have been seen in tetanus muscle where there was no loss of weight. Buzzard and Greenfield [32] illustrate similar fibers in early degeneration of muscles in amyotrophic lateral sclerosis, contrasting them with advanced atrophy in the same disease where many fibers have shrunken in size and others have been replaced by fibrous connective tissue. Froboese [33] found that gastrocnemius muscle undergoing atrophy as a result of being inactivated for from three to five weeks in the relaxed state by plaster bandages, showed an increase in nuclei, in connective tissue, and, in high grade cases (four to five weeks in plaster cast) a typical fatty degeneration with definite disappearance of muscle fibers. Since his preparations were in plaster bandages, there may have been interference with circulation which produced some of the alteration. The duration of his experiments was also longer than ours. In our preparations there was only a slight increase in the number of muscle nuclei in some of the animals, no apparent difference in others and no increase in connective tissue. Since the fibrils in the shortened muscles were not so tightly packed together as normal and the Cohnheim's areas more prominent, it seems possible that there might have been a thinning out of the fibrillar substance in all of the fibers.

The cats and guinea-pigs showed a somewhat different picture from the rats, of both normal and shortened muscle, in that there was a greater difference in the size of fibers in the same specimen. There were numerous small fibers scattered among the larger ones throughout the cross-sections. In the shortened muscle these small fibers retained

31. Lipschutz, A., and Audova, A.: Comparative Atrophy of Skeletal Muscle After Cutting the Nerve and After Cutting the Tendon, J. Physiol. **55**:300, 1921.

32. Buzzard, E. F., and Greenfield, J. G.: Pathology of the Nervous System, London, Constable, 1921, p. 275.

33. Froboese, C.: Histologische Befunde zur Theorie der Muskelatrophie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **35**:683, 1922.

their angular outlines and seemed to be crushed between the larger fibers which had increased in size over the normal and presented a rounded outline. Figure 7 shows the difference in size and shape of the fibers in cat muscle in contracture. As stained with van Gieson's stain, most of the small angular fibers in normal, and the small flattened ones, in contracted muscle, were somewhat darker yellow. Alkaline sudan III as used by Ewald [34] and recommended by Denny-Brown [35] for the study of pale and opaque fibers, was used on frozen sections of the same muscles to find out whether the flattened fibers were red fibers. This stain colors granules in the muscle fibers red, and the remainder of the muscle substance a very light pinkish orange. The flattened fibers on the side of contracture were rich in red granules and stained darker than the large rounded fibers in the same specimens. Since these flattened fibers stained in the manner characteristic of red fibers with sudan III as well as with the usual stains employed for muscle, their identification as such seemed justified. The reason for their failure to swell and maintain a more nearly cylindric form as the pale ones did in the contracted muscles is not apparent.

No fatty degeneration or increase in fat between the fibers could be demonstrated with fat stains.

Though no series of experiments was carried out with the intention of investigating the possibility of recovery, it was noted that the three rats that were allowed to live forty-four days after tenotomy had recovered function in their legs. Two of them were able to walk quite normally, raising their ankles well off the floor, and were able to push back with considerable force against a finger placed behind the toes. The third rat was able to raise the ankle from the floor but not quite so high as the other two, and was not able to push back with the toes with as much force as the others. The shortening of the gastrocnemius in the first two was 6 and 13 per cent, while it was 19 per cent in the third. All three had developed new functioning tendons formed by connective tissue filling in the space between the cut ends of the old tendon. A similar growth of connective tissue between the cut ends of the tendo achillis in dogs has been described by Frantz, Stout and Clarke.[36] In these dogs, only the skin wound was sutured. Function was partially restored when the connective tissue growth had formed a strong enough bond between the ends of the

34. Ewald, W.: Ueber helle und trübe Muskelfasern bei Wirbeltieren und beim Menschen, Abhandl. Senckenberg. Nat. Ges., Frankfort-on-Main, **31**:109, 1912.

35. Denny-Brown, D.: The Histological Features of Striped Muscle in Relation to its Functional Activity, Proc. Roy. Soc. Series B, **104**:371, 1929.

36. Frantz, V. K.; Stout, A. P., and Clarke, W. C.: Surgical Pathology, in Nelson's Looseleaf Surgery, New York, Thomas Nelson & Sons, vol. 1, chapter 4, p. 301.

tendon. Sections were made to determine the nature of the tissue filling the gap in the tendon, but no microscopic study of the muscle was reported.

The histologic picture of the rat's gastrocnemius that was only 6 per cent shorter than its fellow of the opposite side was essentially normal; that of the other two showed only a few of the changes seen in material taken a shorter time after tenotomy. As would be expected with 13 per cent and 19 per cent shortening, cross-sections showed that the fibers of the muscle that had been in contracture were larger than those of the unoperated leg. There was no mottled staining, no loss of alinement of myofibrils and only a few wavy fibers. The chief variation from normal in these muscles was a narrowing of the *J* bands in some of the fibers, giving a very fine striation. Some fibers in the sections had normal spacings of the bands.

Ranson and Ranson [37] carried out a series of experiments to determine the extent to which muscles may recover from tetanus contracture. They produced local tetanus by injection of a sublethal dose of tetanus toxin into one hind limb of rats paired by weight and age. One of each pair was killed at the height of contracture (seven to thirteen days after injection) and the other allowed to live until function returned (fifty-six to one hundred and ten days). All of those killed at the height of contracture showed the typical picture of tetanus contracture, while those in which the function had returned to normal had a normal histologic picture, showing clear cross-striation, no nuclear changes, and no apparent increase in fibrous connective tissue. The absence of marked changes in the rats that had regained function following tenotomy, together with the recovery from tetanus just described, appears to give some support to the idea that the changes seen in the muscle after tenotomy are not irreparable and that with reestablishment of continuity in the tendon and a return of function the structure of the muscle may also become normal. This, however, requires further investigation.

COMMENT

A comparison of the contracture caused by tenotomy with that caused by tetanus toxin reveals several changes common to both and a few that are not. The size and shape of the shortened muscle was the same in both. Increased vascularity characteristic of tetanus muscle in gross aspect was absent in the muscles contracted following tenotomy. The amount of shortening in the two contractures was similar. In the tenotomy series, the gastrocnemius was completely freed from tension by section of the achilles tendon, so that it was free to draw up without restraint. In tetanus contracture, however, the muscle was freed only

37. Ranson, Stephen; and Ranson, S. W.: Recovery from Myostatic Contracture Caused by Tetanus Toxin, Arch. Path. **7**:949 (June) 1929.

from the tension of antagonistic muscles by section of the patellar tendon. Nevertheless, it pulled against the achilles tendon and became as short and thick as the otherwise normal muscles of the tenotomy series that had been completely freed by section of the achilles tendon.

No atrophy was shown by a loss of weight in tetanus, but after tenotomy there was a 20 per cent loss. In making this comparison it must be remembered that the length of time that elapsed in the two series of experiments was different, for the animals with contracture from tetanus were killed in from five to eight days, while the shortest period after tenotomy was sixteen days. Ranson and Ranson [37] found some atrophy even after recovery from tetanus contracture in fifty-six to one hundred and ten days, but not in the seven to thirteen day period in which their controls were killed.

Mottled staining was common to both contractures but occurred in greater extremes in tetanus, for there the beginning degeneration of the contractile substance added to the contrast in the affinity of the different parts of the fibers for the stains. In tetanus, the homogeneous masses in some of the fibers stained very dark, but contracture following tenotomy produced few regions that stained darker than normal, and none of these were the result of degeneration such as was seen in tetanus.

The variations in ratio between the width of isotropic and anisotropic bands were similar in both contractures. However, stretched areas, where the *J* bands had increased to twice their normal width and adjoining portions of fibers where the *Q* bands had approached so close as to nearly obscure the *J* bands, were present in tetanus contracture and absent in that following tenotomy.

Nuclear aggregations which replaced the contractile substance in portions of the sarcolemma tube were found in tetanus but not after tenotomy. This is not surprising, for the introduction of a toxin or other foreign substance might be expected to cause some degeneration even in a short period. Forbus [38] found similar replacement of contractile substance by nuclei in the rectus abdominis muscles in patients with pneumonia and in degeneration experimentally produced by the injection of phenol, alcohol or boiling water. Wisbaum [39] observed it in the psoas and quadriceps in a fatal case of tetanus complicated by pneumonia. Degeneration of portions of the contractile substance into homogeneous or granular masses was not present after tenotomy.

38. Forbus, W. D.: Pathologic Changes in Voluntary Muscle: I. Degeneration and Regeneration of Abdominis Rectus in Pneumonia, Arch. Path. **2**:318 (Sept.) 1926; II. Experimental Study of Degeneration and Regeneration of Striated Muscle with Vital Stains, ibid. **2**:486 (Sept.) 1926.

39. Wisbaum, K.: Histopathologische Nerven- und Muskeluntersuchungen eines Tetanusfalles, Deutsche Ztschr. f. Nervenheilk. **80**:75, 1923.

Connective tissue was not demonstrably increased in either contracture, though nuclei of the wandering cell type were more plentiful in both.

Both contractures had a slight increase in number of muscle nuclei in scattered fibers, but it was not marked in either. In tetanus and after tenotomy, the nuclei in some but not in all specimens appeared a little swollen and stained a little less intensely than normal with hematoxylin.

No difference in the shape of red fibers was observed in rats in either tetanus contracture or in that after tenotomy. Since neither cats nor guinea-pigs were used in the study of tetanus, it is not known whether the inability of the red fibers to retain their cylindric forms against the swelling of the pale fibers is characteristic of contracture or peculiar to contracture after tenotomy in these animals.

None of the changes described account for the inability of these muscles to relax from the shortened state; that is to say, it is not evident why the loss of regular transverse striation should be associated with a shortening of the muscle fibers.

SUMMARY

Myostatic contractures produced in two different ways (by tetanus toxin and by tenotomy) have the following histologic alterations in common: (1) increase in diameter of fibers; (2) more pronounced longitudinal fibrillation; (3) blurred cross-striations; (4) dissociation of membranes holding myofibrils in alinement; (5) wavy contour in some of the fibers; (6) light and dark irregularly outlined bands across some of the fibers, due, in part, to loss of affinity for stains in parts of the fibers; (7) increase in nuclei of wandering cell type; (8) slight increase in muscle nuclei in scattered fibers; (9) no increase in connective tissue that can be demonstrated histologically, and (10) a very irregular histologic picture with the various changes occurring side by side in the same or adjacent fibers.

Myostatic contracture due to tenotomy differs from that caused by tetanus toxin in the following ways:

1. The increased vascularity of tetanus muscle is not present in the contracture due to tenotomy.

2. There is a 20 per cent loss of weight in the gastrocnemius after tenotomy, but no atrophy in tetanus in the period required to produce contracture, i. e., from five to eight days.

3. Degenerative changes consisting of disintegration of contractile substance in some fibers and replacement of contractile substance by aggregations of nuclei within the sarcolemma in others are present in tetanus contracture but not in that due to tenotomy.

PERIOSTEAL LIPOMA

REPORT OF TWO CASES *

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Malignant tumors arising from the periosteum or from structures immediately adjacent to the periosteum and growing out away from the bone without erosion of the bone cortex or invasion of the medullary cavity have been described by Ewing [1] and Codman.[2] At present these tumors are included among the bone tumors in the classification adopted by the Sarcoma Committee of the American College of Surgeons under the heading of periosteal fibrosarcoma. Since the publication of the classification of the Bone Sarcoma Committee much discussion has arisen as to whether these tumors rightly belong with bone tumors, because they seem to have no tendency to involve the bone and because there is no proof that they arise from bone structures.

My purpose in this article is to report two cases of benign tumor which seem to bear the same relationship to bone in that they seem to have developed from the outer layers of the periosteum or the structures immediately adjacent to the periosteum.

REPORT OF CASES

CASE 1.—M. S., a white boy, aged 7, was admitted to the University of California Hospital on July 10, 1919, with a history of tumor of the left arm of about five years' duration that had gradually increased in size. He first came under observation about twenty days before admission to the hospital because of a supracondylar fracture of the opposite or right humerus. The tumor was located on the front of the arm just above the elbow. There was no complaint of pain, tenderness, redness of the skin, etc.; no limitation of motion in the elbow joint; no swelling of the limb below the elbow and no anesthesias or atrophies below the elbow.

Examination showed a rather firm, elastic tumor on the ventral aspect of the left arm just above the elbow. The mass measured 10 by 12 cm. in its greatest and narrowest diameters. The overlying skin was normal but seemed to be firmly adherent to the growth. Lateral mobility of the tumor was moderately free, but movement in the longitudinal axis of the limb was practically nil. Roentgenograms (figs. 1 and 2) showed an apparently encapsulated growth lying immediately

* Submitted for publication, April 2, 1930.

* From the Department of Surgery, University of California.

1. Ewing, James: Review of Classification of Bone Sarcoma, Arch. Surg. **4**: 485 (May) 1922.

2. Codman, E. A.: Bone Sarcoma, New York, Paul B. Hoeber, 1925, p. 5.

against the bone but not eroding it or causing pressure atrophy. There was a question of slight change in shape, that is, a hollowing out of the ventral surface of the humerus. The tumor did not seem to be lobulated, but showed fanlike, radiating markings in the anterioposterior view. This phenomenon was lacking in the lateral view, which showed rather a mottling and an indefinite trabeculation.

Fig. 1.—Lipoma lying against the anterior surface of the humerus. Note the smooth outline, the slight mottling and the saddle-like relationship with the humerus; also the lack of erosion of bone and of thinning of cortex.

Under a tentative clinical diagnosis of ganglion or bursa, the tumor was explored on July 11, 1919. The skin was split over the tumor in the longitudinal axis of the limb. It was necessary to split the biceps muscle in order to get at the tumor, which lay immediately beneath this muscle and against the bone. It overlapped on both sides of the bone and came level with or slightly dorsal to

the posterior surface of the humerus. There was a definite, tough capsule, and the tumor shelled out readily on all sides except where it came in contact with the ventral surface of the bone. Here it was adherent for a distance of from 6 to 8 cm. up to the shaft from the elbow joint over an area from 2 to 3 cm. wide. Sharp dissection was required throughout this area for separation of the tumor

Fig. 2.—Lipoma of the bone on the anterior surface of the humerus. Note the trabeculation and the fanlike arrangement of the fibrous tissue.

from the bone. After removal of the growth there seemed to be a much thickened periosteum remaining, as if a portion of the tumor capsule had been left behind. Inspection of the mass, however, proved that the capsule was intact at all points, but that the tumor was deeply grooved by the humerus. The wound was closed tight, and healing by primary union took place.

The patient was discharged from the hospital seven days after the operation. The ultimate recovery was complete without impairment of the motor or sensory functions and with full motion in the elbow joint. There has been no recurrence.

The pathologic report described a sharply encapsulated, slightly lobulated tumor the cut surface of which was yellowish white, suggesting a large fat content. Microscopic sections showed typical adult, fatty tissue interspersed with rather frequent, heavy strands of connective tissue. The final diagnosis was fibrolipoma.

CASE 2.—F. S., a white boy, aged 6, was admitted to the University of California Hospital on April 11, 1927, with a history of gradual, uniform enlargement of the leg below the right knee for three years with rapid development of a definite mass during the last five or six months. No pain, tenderness, redness or discoloration of the skin, no limping and no impairment of the patient's general health were noted. There was no history of illness, except the usual children's diseases and occasional colds. The height, weight and mentality were normal.

The left leg showed a general bulging just below the knee, and a tumor mass could be felt, estimated to be about 18 by 10 cm. in size and apparently lying in the midst of the muscle of the calf. There was no redness of the skin, but the subcutaneous veins were moderately dilated over the tumor, and there was some dilatation of the veins as high up as the groin. The tumor was of firm consistency, not fluctuant and not bony hard. It could be demonstrated as lying posterior to the tibia and fibula and largely to the tibial side. The patient could move all of the joints of this limb, including those of the toes. There were no swellings of the leg or foot and no sensory changes. All laboratory tests gave normal results, including tests of the urine and stool, complete blood tests and Wassermann examinations of the blood. Roentgenograms (figs. 3, 4 and 5) showed a sharply limited and apparently encapsulated mass lying firmly against the posterior surface of the tibia and causing considerable bowing forward of that bone, together with pressure atrophy of a small area in the cortex of the fibula. There were typical trabeculations and suggestive lobulations. There was no evidence of erosion or thinning of the cortex of the tibia. The epiphyses of both leg bones were normal.

Under a clinical diagnosis of fibrolipoma, the tumor was explored on April 15, 1927. It was found to be a firm, well encapsulated, lobulated tumor lying between the gastrocnemius muscles and the bones. The tumor could be reached best by lateral retraction of the gastrocnemius muscles. It shelled out fairly easily, except where it came in contract with the posterior surface of the tibia. Here it had to be peeled off of the bone, mostly by sharp dissection. After removal of the tumor, the periosteum of the tibia was still intact and seemingly considerably thickened, suggesting that a part of the capsule of the tumor had been left behind, although inspection of the tumor showed that the capsule everywhere was intact. Bleeding was negligible, and the wound was closed without drainage.

The postoperative course was uneventful, except for some swelling of the leg below the wound and the formation of an hematoma. The latter was drained, and the wound healed completely by the twelfth day. The patient was discharged as well and able to walk on April 30, that is, fourteen days after operation. Subsequently there has been no recurrence.

The gross specimen showed a lobulated, bosselated, encapsulated mass measuring 8 by 9 cm. in greatest and shortest diameters. The cut surface had the yellowish appearance of fat, and on macroscopic examination the impression was that it was a lipoma. Sections showed the adult type of fat cells intermixed with a great many rather heavy sheets of dense fibrous tissue. The final diagnosis was fibrolipoma.

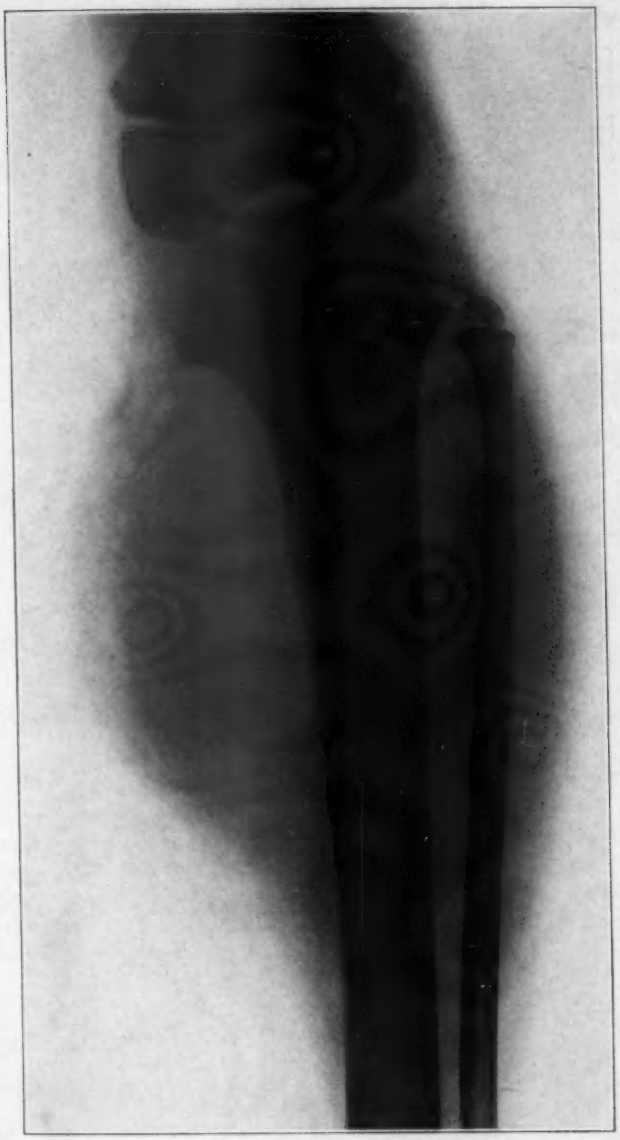

Fig. 3.—Lipoma lying against the posterior surface of the tibia. Note the mottling and the sharp limits of the tumor.

Fig. 4.—Lipoma against the posterior surface of the tibia causing marked bowing of the upper end without erosion or thinning of the cortex.

Fig. 5.—Lipoma of bone against the posterior surface of tibia shown in oblique view. Note the depression on the surface of the fibula. This was erroneously interpreted before operation as atrophy of bone through pressure or erosion. It proved to be a saucer-like depression and the cortex was not thinned.

COMMENT

The foregoing cases presented some difficulties in making a positive clinical diagnosis. The first tumor was erroneously suspected of being a bursa of some sort, because the x-ray picture was the first one of its type the author had encountered. Malignancy was not considered because of the large size of the growth, the intact periosteum, the very sharp limits of the tumor and the normal condition of the overlying skin and soft parts. At operation the tumor capsule and periosteum merged together so completely that there was no line of cleavage. The tumor had to be separated from the bone by sharp dissection, what seemed to be the outer layers of the thickened periosteum being taken with the tumor. The close blending of the periosteum and tumor capsule is not easily explainable on the basis of contact alone, and there were no fascial planes at this point from which the tumor could originate.

The second tumor was clinically diagnosed lipoma because of the similarity between its x-ray picture and that in the first case. The characteristics in common between the two pictures which pointed to a diagnosis of lipoma were the peculiar form of trabeculation, the very sharp limits and the tendency to alter the shape of the bone by pressure without erosion or bone atrophy. The second case showed what seemed to be an erosion of the fibula, and this caused some doubt regarding the actual benignancy of the growth. The rest of the picture, however, was so overwhelmingly suggestive of benignancy that the area of seeming erosion was disregarded as probably artefact. This was explained at operation, when it was discovered that the flattening of the cortex of the normal fibula caused a shallow, saucer-like depression to resemble erosion when viewed tangentially. Again the tumor capsule had to be separated from the periosteum by sharp dissection, but in this case there were fascial planes from which the tumor might have arisen. Still the total lack of lines of cleavage between the capsule and the periosteum was unexplained.

One would not be justified perhaps in contending that these tumors be called periosteal lipoma or that tumors of this sort should be included under the classification of tumors of the bone. On the other hand, it might not be wholly illogical to look on tumors of this sort as belonging to a group that constitutes the benign counterpart of a malignant group to which the so-called periosteal fibrosarcoma belongs.

THE EFFECT OF PERICARDIOSTOMY ON THE MECHANICS OF THE CIRCULATION*

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Since the time when Billroth characterized the operation of tapping the pericardium as "a surgical frivolity and a prostitution of surgical skill," the pericardium has assumed a more important place in surgery. The pericardial cavity has been aspirated for fluid, and it has been incised for pus. It has been opened for the suture of cardiac wounds, for the removal of foreign bodies and for relief from valvular stenoses. The pericardium has been excised when involved by neoplasms. It has been excised, sometimes with the precordial ribs, for adhesive pericarditis and for cardiac hypertrophy. It is apparent that the pericardium has entered the domain of surgery for numerous reasons, and we believe that a fuller appreciation of its pathologic physiology will give it a place of even greater importance than it has held in the past.

Despite the notable progress that has been made along these various lines of endeavor, we have been unable to find, even after an extensive review of the literature, any experimental study of the secondary effects on the mechanics of the circulation brought about by exposing the heart to atmospheric pressure. The only reference that could be found was in an article on experimental pericarditis by Shipley and Horine,[1] in which the following interesting statement appeared: "Because the pressure everywhere within the thorax, except in the lung itself, is lower than atmosphere, one's curiosity is raised as to the effect of atmospheric pressure on the heart after pericardiotomy. Certainly the function of the wall of the chest is to maintain a negative pressure within the thorax, and it is not unreasonable to suspect that the heart may be disturbed by exposure to atmospheric pressure."

This paper is based on experiments carried out to determine what effects on the mechanics of the circulation were produced by exposure of the heart to atmospheric pressure.

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* Submitted for publication, April 7, 1930.

* From the Laboratory of Surgical Research, the Lakeside Hospital and the Western Reserve University School of Medicine.

* Read before the Physiological Section of the Federation of American Society for Experimental Biology, Chicago, March 27, 1930.

1. Shipley, A. M., and Horine, C. F.: Experimental Pericarditis, Arch. Surg. **18**:386 (Jan.) 1929.

METHOD

The determinations that we considered important in a study of this problem were: arterial pressure, venous pressure and cardiac output.

The method of determining cardiac output was by means of the Fick principle. Before a dog was used for experimentation, he was trained to lie quietly on a table for long periods of time. Male dogs were selected because the pulse rate of the male is more stable than that of the female. After a preliminary period of quiet a rubber mask, devised by Blalock,[2] was placed over the nose and mouth, and this was connected to the Benedict spirometer. The oxygen consumption per minute, reduced to standard conditions of temperature and pressure, was determined by taking the average of a six minute curve. Samples of blood were then drawn under oil from the right and left ventricles. The skin and the pleura were usually infiltrated with a few drops of procaine hydrochloride. The oxygen content of 1 cc. of these specimens was determined immediately by means of the Van Slyke-Neill [3] manometric apparatus. These specimens were analyzed in duplicate, and if the variation in pressure readings exceeded 0.15 mm. of mercury, either another set of determinations in duplicate was taken or the specimens were discarded.

According to the Fick formula:

$$\frac{\text{Cubic centimeters of } O_2 \text{ consumed per minute}}{\text{Amount of } O_2 \text{ taken up by 1 cc. of blood in passing through the lungs}} = \text{Cubic centimeters of blood passing through the lungs per minute.}$$

This may be expressed as follows: The oxygen consumption per minute in cubic centimeters divided by the difference in oxygen content of 1 cc. of arterial blood and 1 cc. of venous blood equals the amount of blood in cubic centimeters put out by the heart per minute.

The foregoing principle and method have been used for much experimental work in the last few years. If the determinations are done under satisfactory conditions, the results will agree with surprising accuracy, within a variation of 10 per cent.[4] Occasionally a wide deviation in results is obtained, but this is due either to a mixture of ventricular blood or to the fact that the dog has not maintained his basal level.

The dog does not possess an area on the thoracic wall in contact with the pericardium similar to the "triangle of safety" in the human being, which was described by Voinitsch-Sianojentzky.[5] To open the pericardium without opening the chest, it was necessary to suture the pericardium to the thoracic wall as a preliminary step before opening it to atmospheric pressure (figs. 1 and 2).

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2. Blalock, A.: Rubber Mask for Determination of Oxygen Consumption of Dog, J. Lab. & Clin. Med. **12**:378 (Jan.) 1927.

3. Van Slyke, Donald D., and Neill, James M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement: I, J. Biol. Chem. **61**:523, 1924.

4. Marshall, E. K., Jr.: Studies on the Cardiac Output of the Dog, Am. J. Physiol. **77**:459, 1926.

5. Voinitsch-Sianojentzky, A.: Die Operationen der Eröffnung des Herzbeutels, und ihre anatomischen Grundlagen, Arch. f. path. Anat. **151**:380, 1898.

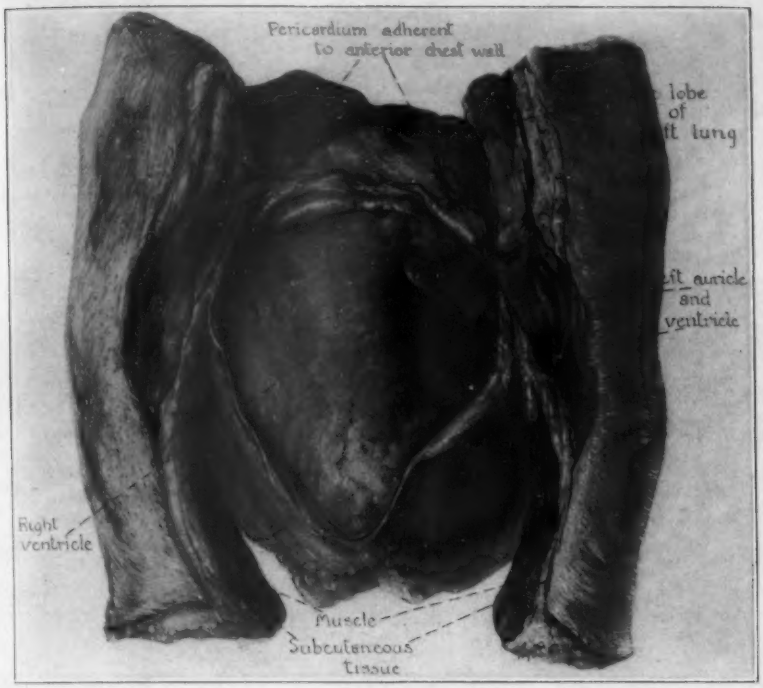


Fig. 1.—The pericardium had been attached to the thoracic wall and the pericardial cavity opened to the exterior. The drawing shows a portion of the thoracic wall and the pericardium bisected.

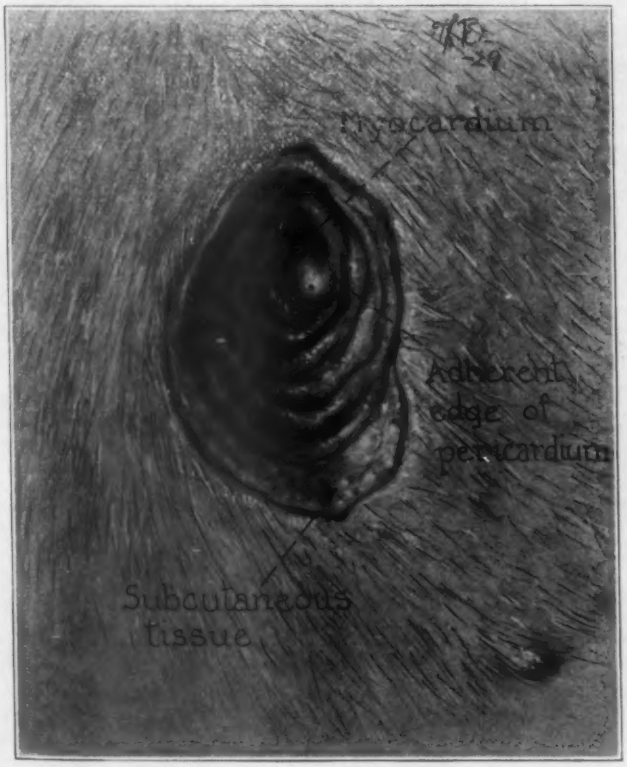


Fig. 2.—The pericardiostomy as seen from the exterior.

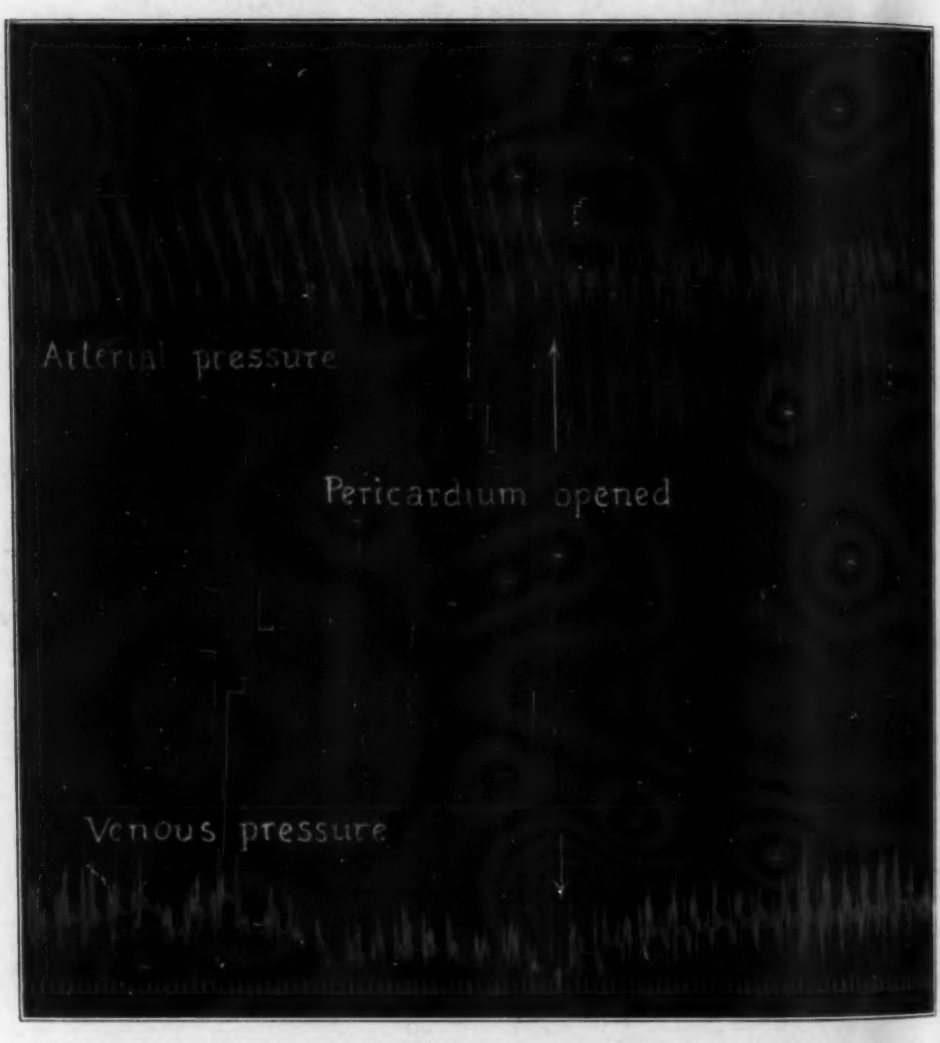
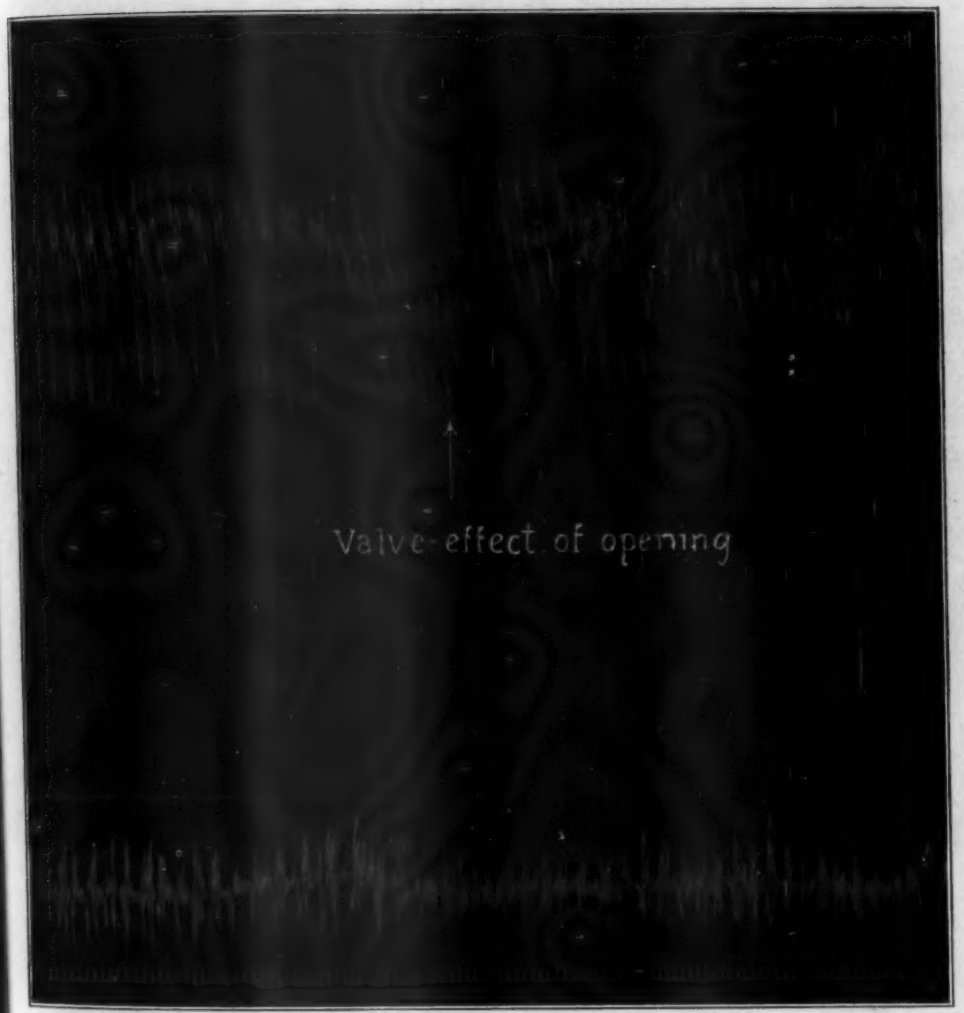


Fig. 3.—Graph showing the arterial and venous pressures before and after opening the pericardial cavity to the atmosphere. When the pericardial cavity was opened, the arterial



pressure fell from 20 to 30 mm. of mercury and the venous pressure rose. The fluctuations in arterial pressure occurred when the opening into the pericardial cavity was partially obstructed.

BLOOD PRESSURE DETERMINATIONS

EXPERIMENT 1.—On Aug. 24, 1929, a mongrel bull-dog, weighing 21.6 Kg., was anesthetized with ether. Three inches (7.6 cm.) of the left fifth rib were resected, and the pericardium was securely sutured to the thoracic wall over an area about 4 cm. in diameter. The muscle, subcutaneous tissue and skin were approximated with silk sutures.

On September 19, the dog was in good condition. The wound had healed.

On November 8, 1 Gm. of sodium *iso*-amylethylbarbiturate (amytal) was injected intravenously for anesthesia. The left femoral artery was cannulated and connected to a mercury manometer. The left jugular vein was cannulated close to

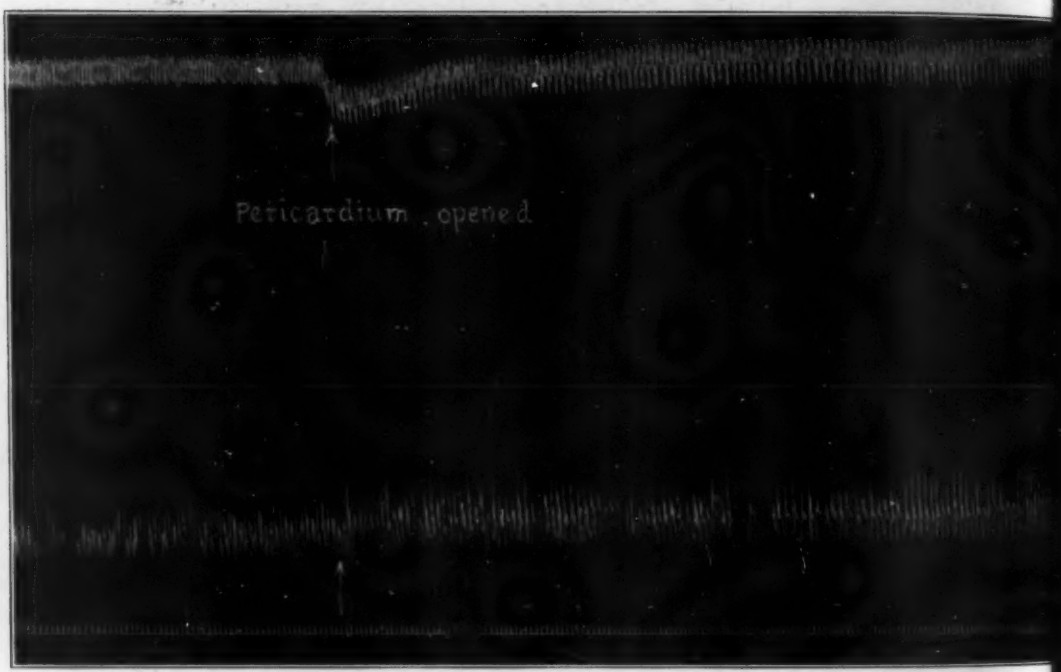


Fig. 4.—When the pericardial cavity was opened to atmospheric pressure, the arterial pressure fell 10 mm. of mercury, and after twenty-eight seconds regained its former level. There was a sustained rise in the venous pressure.

its junction with the innominate and connected to a Marey tambour. Tracings of arterial and venous pressures were obtained.

The scar over the left fifth rib was incised, and the pericardium was opened. When the pericardium was opened, an immediate fall in arterial pressure and a rise in venous pressure took place (fig. 3). The fall in arterial pressure measured from 20 to 30 mm. of mercury. These pressure changes were sustained. The egress and ingress of air in the pericardial cavity were demonstratable, and when this passage of air was obstructed by placing the soft tissues in the opening of the pericardium the arterial pressure fell still further. Within a few seconds, the arterial pressure swung to a higher level and then fell again.

The foregoing experiment was repeated.

EXPERIMENT 2.—On June 6, 1929, a dog weighing 21 Kg. was anesthetized with ether, and the pericardium was sutured to the thoracic wall.

On August 26, under ether anesthesia, a femoral artery and a jugular vein were cannulated, and pressure determinations were taken. The pericardium was then opened to atmospheric pressure. There occurred immediately a slight but definite fall in arterial pressure and a rise in venous pressure.

EXPERIMENT 3.—On June 28, 1929, the pericardium was sutured to the thoracic wall, and subsequently the cavity was opened to atmospheric pressure. The dog was utilized for a long series of cardiac output determinations (see succeeding material).

The pericardiostomy wound healed, and the pericardial cavity became sealed from atmospheric pressure. Under ethyl carbamate anesthesia, the left femoral

Fig. 5.—The positive atmospheric pressure within the pericardial cavity and the negative pressure within the pleural space produced some dilatation of the pericardial cavity. The latter is more capacious than normal.

artery and the left jugular vein were cannulated. The former was connected to a mercury manometer and the latter to a Marey tambour. Pressure tracings were taken. The thoracic scar was incised, and the pericardial cavity was opened to atmospheric pressure. As soon as air entered the pericardial cavity, the arterial pressure fell and the venous pressure rose (fig. 4). The fall in arterial pressure measured about 10 mm. of mercury and was transient, the pressure regaining its former level in twenty-eight seconds. The rise in venous pressure was sustained.

At necropsy the pericardial cavity was definitely more capacious than normal. It was increased in its transverse diameter, and it extended superiorly over the great vessels at the base of the heart, producing a condition similar to the dilatation that occurs in cases of pericardial effusion (fig. 5).

EXPERIMENT 4.—On June 7, 1929, the dog weighed 24 Kg. The first stage operation was carried out under ether anesthesia.

On June 28, arterial and venous pressure determinations were made under ethyl carbamate anesthesia. When the pericardium was opened to atmospheric pressure, the arterial pressure fell 20 mm. of mercury and the venous pressure slightly but definitely increased. The arterial pressure regained its former level in twenty seconds; the venous pressure remained elevated throughout the experiment. The dog was killed.

COMMENT

It is apparent from the preceding experiments that when the pericardial cavity was opened to atmospheric pressure, a fall in arterial pressure and a rise in venous pressure occurred. These pressure changes were always definite. In one experiment the fall in arterial pressure was slight, measuring from 6 to 8 mm. of mercury. In another experiment, a fall of 10 mm. occurred, and this fall in pressure persisted twenty-eight seconds before the former level was regained (fig. 4). In another experiment, the fall in arterial pressure measured from 20 to 30 mm. of mercury, and this pressure change was sustained throughout the experiment (fig. 3). When the opening into the pericardial cavity was closed by placing soft tissues into it, fluctuation in pressure occurred. This fluctuation was probably related to changes in intrapericardial pressure brought about by respiration, but these changes did not seem to synchronize with the respiratory cycle. In each experiment the venous pressure showed a definite increase when the pericardium was opened, and the rise was maintained throughout the experiment.

The explanation of these pressure changes is apparent. As the pericardium is a collapsible structure, it readily yields to the intrathoracic pressure changes that accompany inspiration and expiration. The intrapericardial pressure, therefore, may be assumed to be the same as the intrathoracic pressure. These recurring pressure changes (from —4.64 mm. at the end of quiet inspiration to —3.02 mm. of mercury at the end of expiration [6]) play an important rôle in the filling of the heart. Because of the negative pressure in the thorax, the pressure in the great veins at the base of the heart is very low. According to Burton-Opitz,[7] the pressure in the superior vena cava near the auricle in the dog was —2.96 mm. of mercury.

When the pericardium is opened to the atmosphere, the negative intrapericardial pressure is changed to the positive atmospheric pressure This increased intrapericardial pressure expresses itself in two ways. It has a dilating effect on the pericardium and increases the size of the cavity in a manner similar to that produced by pericardial effusions. It also exerts a compression effect on all intrapericardial structures.

6. Aron, quoted by Howell: Physiology, Philadelphia, W. B. Saunders Company, 1915, p. 659.

7. Burton-Opitz, R.: Venous Pressures, Am. J. Physiol. **9**:198, 1903.

including the ventricles, the auricles and the great arteries and veins. Of these structures, the intrapericardial portions of the superior and inferior venae cavae carry the least pressure, and presumably it is on these great veins that the compression effect of atmospheric pressure is relatively the greatest. From a consideration of the usual negative pressure existing within the venae cavae, i. e., the portion within the pericardial cavity, one would expect collapse of the great veins. This, however, is undoubtedly prevented by the immediate accumulation of blood in the great veins assembling a transmitted pressure from the periphery. This pressure is sufficient to drive the blood into the heart against the positive atmospheric pressure within the pericardium.

The pressure changes obtained in the foregoing experiments suggest that an increase in the venous pressure is necessary to overcome the positive intrapericardial pressure of the atmosphere. The slight decrease in arterial pressure indicates that this positive atmospheric pressure

TABLE 1.—*Cardiac Output Determinations in Experiment 5*

	Oxygen Consumption, Cc. per Minute	Oxygen Content, per Cent by Volume, 1 Cc. of Blood		Arterial-Venous Difference	Cardiac Output,* Cc. per Minute	Pulse Rate
		Arterial	Venous			
Before opening pericardium...	87.4	20.80	16.93	3.87	2,258	144
After opening pericardium....	88.9	21.48	15.85	5.63	1,579	192

* The fall in the cardiac output was 30 per cent.

constitutes a handicap to the cardiac function. This is brought about chiefly by the impairment to the filling of the heart, although the direct pressure increment on the ventricles and auricles may also be a factor. The problem was studied further by cardiac output determinations taken before and after the pericardial cavity was opened to the atmosphere.

CARDIAC OUTPUT DETERMINATIONS

EXPERIMENT 5.—On Sept. 5, 1929, a male mongrel dog, weighing 11 Kg., was anesthetized with ether and the pericardium was sutured to the left thoracic wall, as described in preceding experiments.

On October 24, under sodium *iso*-amylethylbarbiturate anesthesia, the left femoral artery and the left jugular vein were cannulated and attached to a mercury manometer and a Marey tambour, respectively. An oxygen consumption curve, and samples of the right and the left ventricular blood were taken, before and after the pericardium was opened to atmospheric pressure. The dog was killed by ether narcosis.

Immediately after the pericardial cavity was opened, the arterial pressure dropped from 130 to 120 mm. of mercury, and the venous pressure showed a slight but definite rise. The arterial pressure regained its former level in a few seconds, but the rise in venous pressure was maintained throughout the experiment.

The marked drop in the cardiac output obtained in experiment 5 made us question the veracity of results obtained from experiments in which the animals were killed. One of the complications met with in experiments similar to the preceding was a pneumothorax due to the leakage of air through puncture wounds in the pericardium made by the aspirating needle.

The following series of experiments in which the animals were allowed to recover were carried out.

EXPERIMENT 6.—On a male mongrel collie weighing 16.5 Kg. cardiac output determinations were carried out to determine the normal.

On March 30, 1929, under ether anesthesia, about 5 cm. of the left fourth rib and costal cartilage was removed. The pericardium was sutured to the thoracic wall, and the muscle, subcutaneous tissue and skin were approximated in layers.

TABLE 2.—*Cardiac Output Determinations in Experiment 6*

	Oxygen Consumption, Cc. per Minute	Oxygen Content, per Cent by Volume, 1 Cc. of Blood		Arterial-Venous Difference	Cardiac Output, Cc. per Minute	Pulse Rate
		Arterial	Venous			
Jan. 16, 1929	108.22	17.89	13.07	4.82	2,245	96
Jan. 29, 1929	100.61	16.78	13.03	3.75	2,683	68
March 8, 1929	126.64	19.27	13.87	5.40	2,345	100
March 8, 1929	123.99	20.85	14.62	6.23	1,990	88
March 27, 1929	98.40	19.63	15.75	3.88	2,537	60
March 28, 1929	86.58	19.35	15.34	4.01	2,159	60
On March 30, the pericardium was sutured to the thoracic wall						
April 12, 1929	79.68	19.50	15.76	3.80	2,097	88
April 17, 1929	91.52	19.44	15.76	3.68	2,487	80
April 29, 1929	103.48	21.51	16.92	4.60	2,250	80
On May 15, the pericardial cavity was opened to atmospheric pressure						
May 17, 1929	97.94	16.92	11.91	5.00	1,959	124
May 18, 1929	91.94	15.74	9.43	6.30	1,459	88
May 19, 1929	87.26	13.08	4.67	8.41	1,039	100
May 20, 1929	104.08	15.21	4.82	10.39	1,001	100
May 22, 1929	96.18	23.18	12.03	11.15	863	100

Cardiac output determinations were repeated.

On May 15, the dog was in good condition, weighing 17 Kg. Morphine, 0.16 Gm., was given. The scar over the left fourth rib was infiltrated with procaine hydrochloride, and the pericardium was incised for about 1 cm., producing a free communication with the atmosphere. The conus arteriosus was visible, and specimens of blood from the right and left ventricles could be obtained easily through the pericardiostomy opening. Cardiac output determinations were repeated, but purulent pericarditis developed after a few days, and this terminated the experiment.

On May 23, the weight of the dog at necropsy was 14.4 Kg. The pericardial cavity contained about 75 cc. of creamy pus. The heart seemed to be dilated, and the epicardium was covered with a thick coating of fibrin and pus. The pericardial cavity was definitely more capacious than normal. The pleural cavity was well sealed off and showed no evidence of infection. There was a small adhesion between the left middle lobe of the lung and the scar in the thoracic wall. The lungs and the abdominal organs appeared normal. A few days before death edema of the hind legs developed.

The average of the cardiac output determinations before and after the pericardium was sutured to the thoracic wall is 2,326 and 2,278 cc., respectively. A cardiac output determination carried out two days after the pericardium was opened showed a decrease of 319 cc., or 14 per cent, from the previous determinations. Subsequent determinations showed a progressive decrease in cardiac output, but these determinations are probably of no significance because of the development of purulent pericarditis.

EXPERIMENT 7.—On a male collie weighing 15.12 Kg. cardiac output determinations were made to determine the normal.

On Feb. 12, 1929, under ether anesthesia, about 4 cm. of the left sixth rib and costal cartilage was removed. The pericardium was sutured to the thoracic

TABLE 3.—*Cardiac Output Determinations in Experiment 7*

	Oxygen Consumption, Cc. per Minute	Oxygen Content, per Cent by Volume, 1 Cc. of Blood		Arterial-Venous Difference	Cardiac Output, Cc. per Minute	Pulse Rate
		Arterial	Venous			
Jan. 27, 1929	116.84	18.12	12.88	5.26	2,221	83
Feb. 2, 1929	127.57	18.04	12.47	5.57	2,290	74
On February 12, the pericardium was sutured to the thoracic wall						
March 4, 1929	72.72	18.05	14.35	3.70	1,965	78
March 6, 1929	121.28	17.75	11.91	5.84	2,077	88
March 19, 1929	104.24	17.92	12.28	5.64	1,848	80
March 21, 1929	109.70	18.72	13.38	5.34	2,054	88
On March 21, the pericardial cavity was opened to atmospheric pressure						
March 21, 1929	104.72	19.30	12.83	6.47	1,619	72
March 22, 1929	91.11	17.38	10.96	6.42	1,419	140
March 24, 1929	119.43	18.77	11.35	7.42	1,610	110

wall over an area about 3 cm. in diameter. The muscle, subcutaneous tissue and skin were approximated with silk sutures.

Cardiac output determinations were repeated.

On March 21, the wound had healed and the dog was in good condition. The scar was infiltrated with procaine hydrochloride, and an opening about 2 cm. in diameter was made into the pericardial cavity. Cardic output determinations were carried out. Subsequently, the dog developed pneumothorax due to the leakage of air through the small holes produced by the aspirating needle.

The dog died on March 25. The left pleural cavity was distended with air, and the left lung was completely collapsed. The right lung was not collapsed. The pericardium was firmly adherent to the thoracic wall to which it had been sutured. The pericardial cavity contained a little frothy fluid, and there was evidence of an early pericarditis. The heart was not dilated. The pericardium was slightly thickened, and the pericardial cavity was larger than normal. The abdomen contained a small amount of free fluid.

It is seen from the determinations in table 3 that there was a slight drop in the cardiac output following the attachment of the pericardium to the thoracic wall. The determinations taken after the pericardium

was opened unfortunately were complicated with pneumothorax, which developed from the small leaks in the pericardium produced by the aspirating needle.

The first determination made immediately after the pericardium was opened, however, seemed to have been free from this possible source of error. If this was so, there was a decrease in the cardiac output of 18 per cent when the pericardium was opened to atmospheric pressure.

The same unfortunate complications developed in another experiment, in which twenty determinations had been carried out. There were no readings sufficiently accurate after the pericardium was opened to warrant a record of this experiment.

TABLE 4.—*Cardiac Output Determinations in Experiment 3*

	Oxygen Consumption, Cc. per Minute	Oxygen Content, per Cent by Volume, 1 Cc. of Blood		Arterial-Venous Difference	Cardiac Output, Cc. per Minute	Pulse Rate
		Arterial	Venous			
Feb. 25, 1929	105.81	15.98	10.87	5.11	2,071	68
March 1, 1929	116.72	18.93	12.45	6.48	1,801	68
March 6, 1929	107.84	15.40	10.43	4.97	2,170	80
On March 18, the pericardium was sutured to the thoracic wall						
April 1, 1929	103.14	16.43	11.06	5.37	1,921	50
April 9, 1929	89.07	17.09	12.44	4.65	1,913	60
On June 4, the pericardial cavity was opened to atmospheric pressure						
June 5, 1929	107.79	18.18	11.40	6.78	1,590	72
June 6, 1929	79.14	16.10	11.08	5.02	1,576	92
June 7, 1929 a.m.	85.23	16.98	10.96	6.02	1,415	96
June 7, 1929 p.m.	93.49	16.50	10.35	6.15	1,520	96
June 12, 1929	96.16	14.68	8.54	6.14	1,567	92
The wound had healed and the opening into the pericardial cavity had closed						
June 19, 1929	95.41	14.99	9.96	5.03	1,897	72

The two succeeding experiments are conclusive.

EXPERIMENT 3.—Determinations of normal cardiac output were made on a male collie weighing 14 Kg.

On March 18, 1929, under ether anesthesia, about 4 cm. of the left fifth rib was removed, and the pericardium was sutured to the thoracic wall so that an area about 4 cm. in diameter came into contact with the wall. On June 4, the dog was given 0.16 Gm. of morphine, and the scar was infiltrated with procaine hydrochloride. The pericardial cavity was opened to atmospheric pressure. The dog had been in good condition throughout the experiment, and on June 7 cooperated perfectly for cardiac output determinations. On June 19, the wound had healed so that the opening into the pericardial cavity had become completely obliterated. The condition at this time was equivalent to that before the pericardial cavity was opened (June 4). On June 28, under ethyl carbamate anesthesia, the left femoral artery and the jugular vein were cannulated to a mercury manometer and a Marey tambour, respectively. The pericardium was again opened to atmospheric pressure, and the effect on the arterial and the venous pressures was recorded (fig. 4).

The dog was killed and necropsy was carried out. There were no adhesions between the heart and the pericardium. On the epicardium and the parietal pericardium were a number of small plaques of fibrin covered by a smooth glistening surface. The pericardial cavity was increased in size. This dilatation was similar to that produced by pericardial effusions. There was no evidence of infection. The lungs, the pleural cavities and the abdomen were normal. There was no edema and no evidence of an impaired circulation.

It appears from the determinations in table 4 that the cardiac output decreased about from 300 to 400 cc. per minute when the pericardial cavity was opened to atmospheric pressure. This represents a decrease

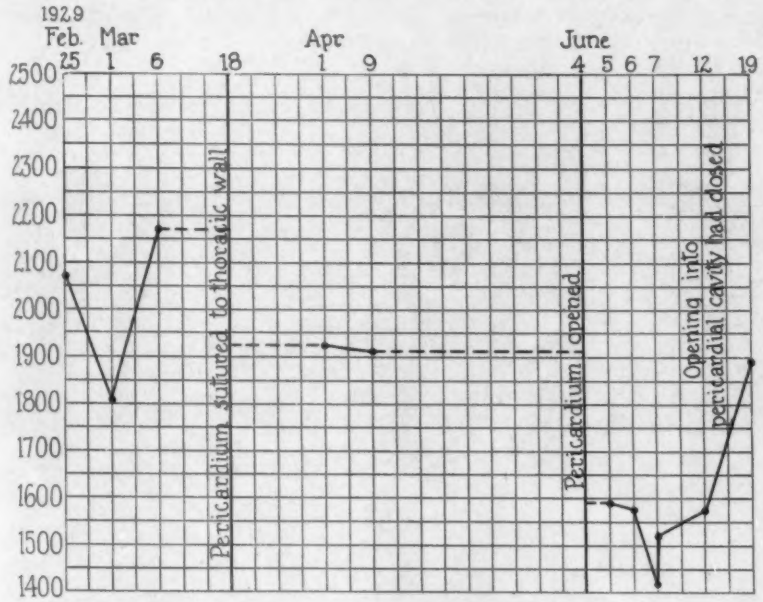


Fig. 6.—Chart showing the minute volume output of the heart in cubic centimeters before and after the pericardium was sutured to the thoracic wall, after the pericardial cavity was opened to atmospheric pressure and after this opening had closed.

of about 20 per cent in the minute output of the heart. It was shown also that after the opening into the pericardial cavity became obliterated by the healing of the wound the cardiac output returned to its former level (fig. 6). It also appears from the analyses that the oxygen content of both the left ventricular and the right ventricular blood decreased after the pericardium was opened, and that this decrease was more marked in the mixed venous blood.

EXPERIMENT 8.—This dog was a female mongrel weighing 15.0 Kg. On Sept. 4, 1929, under ether anesthesia, 3 cm. of the left fifth rib was removed, and the pericardium was sutured to the thoracic wall so that an area of the pericardium about 3 cm. in diameter came into contact with the thoracic wall.

On December 16, the dog cooperated poorly for cardiac output determination. Many of the determinations are not included because of the great fluctuation from the basal level. Morphine or sodium *iso*-amylethylbarbiturate given intravenously was used as a sedative for some of the studies. The determinations in which drugs were used are so labeled. The cardiac output determinations that were carried out immediately after the pericardial cavity was opened were complicated by pneumothorax. A sufficiently long interval was given for the pneumothorax to disappear, and care was taken subsequently not to pass the aspirating needle through the pericardium in taking samples of blood.

On Jan. 2, 1930, a snugly fitting catheter was inserted into the opening of the pericardium and attached to a tambour and writing lever. The egress of air from the pericardial cavity with expiration could be easily felt on the hand. The graph records the passage of air synchronous with respirations (fig. 7). When attached to a water manometer having a bore of 4 mm., the fluctuations in the column of water averaged 8 cm.

On January 21, the wound had healed so that the opening into the pericardial cavity had become closed.

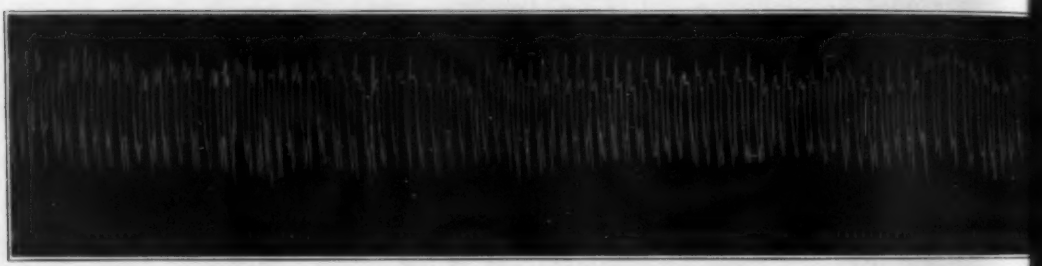


Fig. 7.—Graph indicating the passage of air through the opening into the pericardial cavity.

TABLE 5.—*Cardiac Output Determinations in Experiment 8*

	Oxygen Consumption, Cc. per Minute	Oxygen Content, per Cent by Volume, 1 Cc. of Blood		Arterial-Venous Difference	Cardiac Output, Cc. per Minute	Pulse Rate	
		Arterial	Venous				
Sept. 20, 1929...	97.24	16.65	12.54	4.11	2,366	98	A* 0.5 Gm.
Oct. 1, 1929....	78.94	17.97	14.72	3.25	2,429	140	A 0.5 Gm.
Oct. 10, 1929....	127.85	18.52	12.49	6.03	2,120	116	A 0.5 Gm.
Nov. 15, 1929...	122.96	19.90	14.63	5.28	2,329	92	No drugs
Dec. 7, 1929....	108.46	20.14	14.39	5.76	1,883	80	M†0.16 Gm.
Dec. 16, 1929....	79.78	19.67	16.39	3.28	2,432	96	A 0.5 Gm.
The pericardial cavity was opened to atmospheric pressure							
Dec. 28, 1929....	116.19	21.04	13.59	7.45	1,560	144	No drugs
Dec. 31, 1929....	100.36	19.51	13.96	5.55	1,808	150	No drugs
Jan. 2, 1930.....	73.88	15.77	13.30	4.47	1,653	132	A 0.6 Gm.
On January 21, the wound had healed and the opening into the pericardial cavity had closed							
Jan. 21, 1930...	95.87	15.93	12.15	4.79	2,001	126	A 0.5 Gm.
Jan. 24, 1930...	83.77	17.79	14.05	3.74	2,240	112	No drugs
Jan. 25, 1930...	90.18	17.47	13.25	4.22	2,137	92	No drugs

* A indicates sodium iso-amylethylbarbiturate anesthesia.
† M indicates morphia anesthesia.

On January 25, the experiment was finished. The dog was in good condition and was not killed.

From the determinations in table 5 it seems that although there were some wide fluctuations, the minute output of the heart fell about 20 per cent when the pericardial cavity was opened to atmospheric pressure. This loss in minute volume output was almost entirely regained after the pericardial cavity became closed from atmospheric pressure (fig. 8).

SUMMARY OF DATA

From the experiments it may be concluded that when the pericardial cavity was opened to atmospheric pressure, there occurred: 1. A definite

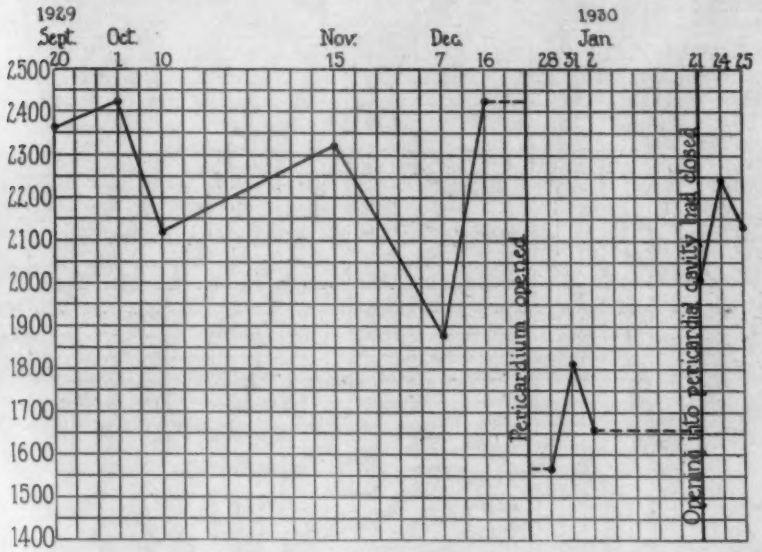


Fig. 8.—Chart showing the minute volume output of the heart in cubic centimeters before and after opening the pericardial cavity to atmospheric pressure and after the opening in the pericardial cavity closed.

sustained rise in venous pressure. 2. A fall of from 8 to 30 mm. of mercury in the arterial pressure. This decrease in pressure was sustained in one experiment; in others it was transient. 3. A decrease of from 15 to 30 per cent in the minute volume output of the heart. There was a return to almost normal minute volume output following closure of the pericardial opening.

The mechanism producing these changes is a pressure phenomenon. Atmospheric pressure acts as an air tamponade on the heart and the great vessels within the pericardial cavity. It also produces dilatation of the pericardial cavity similar to that produced by the effusion of fluid.

We should like to name this mechanism pneumocardiac tamponade.

CLINICAL APPLICATION OF THIS MECHANISM

This mechanism may play an important rôle in all cardiac and pericardial surgery. The disturbance to the circulation brought about by exposing or opening the pericardial cavity has been observed by surgeons, but the possible effect of atmospheric pressure has never been considered a factor in the development of cardiac failure occurring at operation when these structures were exposed. Its deleterious effect may well be a vital factor in the cases in which the circulation

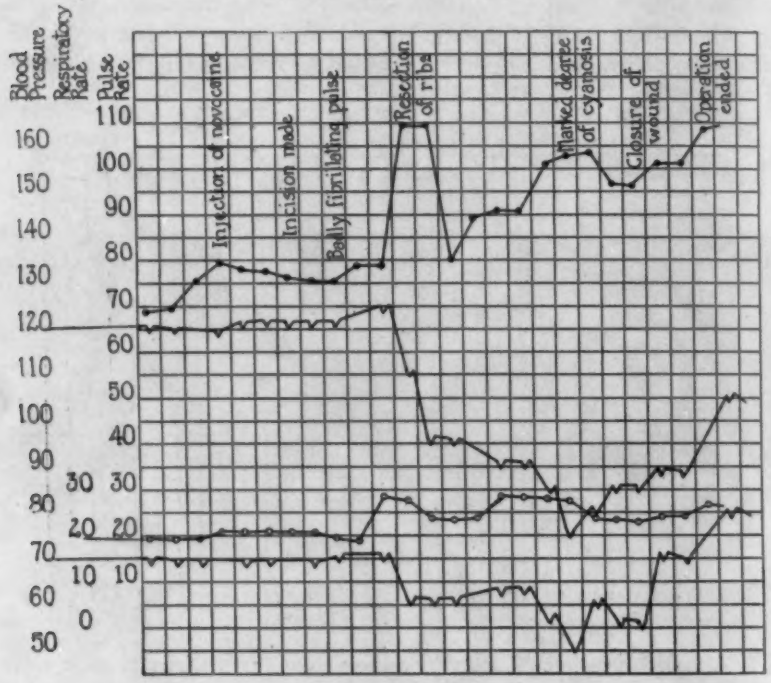


Fig. 9.—Chart of the pulse rate, blood pressure and respiration taken during the resection of the precordial ribs under local anesthesia in a patient with serious decompensation.

is just adequate to maintain life. In such cases, this additional handicap placed on the heart might prove fatal. Such a case is recorded briefly below:

A white man, aged 25, entered the Lakeside Hospital with the complaint of pain over the precordium. At the age of 7 he had had chorea; at 14 he had noted dyspnea; at 20 he had been subjected to sharp stabbing pains localized beneath the left clavicle. For several years he had been an invalid suffering from heart disease, confined to his home and later, to bed.

When admitted to the hospital, the patient appeared to be in a serious condition. He was dyspneic when recumbent; the finger tips and the lips were

cyanotic, and the patient was undernourished. The heart was fibrillating; the rate at the wrist was 70 per minute. The systolic blood pressure was 120 and the diastolic 65. There was an anterior bulge of the precordium. A marked precordial impulse was present. A prolonged systolic murmur and a presystolic thrill and murmur were recorded over the apex. The heart was greatly enlarged, and under the fluoroscope it seemed to be fixed in position. Râles were heard at the base of each lung. Some enlargement of the liver and slight edema of the ankles were present.

The diagnosis of rheumatic heart disease with mitral stenosis and insufficiency was made. The presence of adhesive pericarditis was suspected. For relief from such adhesions and also as a decompression for the enlarged heart, the Brauer operation of cardiolysis was carried out on Sept. 14, 1929.

Under procaine hydrochloride anesthesia, 5 inches (12.7 cm.) of the fourth rib and about 6 inches (15.24 cm.) of the fifth and sixth ribs on the left were removed by subperiosteal resection. The pericardium was incised for the purpose of exploration, but no adhesions were found. The patient withstood the procedure poorly. The blood pressure fell, the pulse rate increased, and the cyanosis became more pronounced. The chart kept by the anesthetist (fig. 9) shows the fall in blood pressure, the decrease in pulse pressure and the rapid pulse rate. It is seen that the fall in pressure occurred approximately at the time when the bony framework was being removed and the pericardium exposed. After the operation was complete, the blood pressure remained low, the pulse rate rapid and the cyanosis extreme. Death occurred twelve hours later.

The tamponade effect produced by atmospheric pressure may be exerted in various types of operation. These include operations on the heart and pericardium and also certain operations on the anterior thoracic wall and mediastinum. It should be noted that the atmospheric pressure can be transmitted on the heart without opening the pericardium. In the selection of cases for operation, the heart should possess a certain reserve power capable of withstanding this tamponade effect.

A REVIEW OF UROLOGIC SURGERY

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(Concluded from p. 866)

URETHRA

Ruptures.—Higgins [25] stated that there are three types of rupture of the urethra: rupture of the pendulous urethra, rupture of the bulbous urethra and rupture of the intrapelvic urethra. The most common type of rupture is that of the bulbous urethra. The symptoms occurring immediately after this type of rupture usually are pain, hemorrhage from the meatus, difficulty or inability to urinate, tenderness and tumefaction. Perineal hematoma may be present. The degree of trauma is not always indicated by the severity of the symptoms. Although inability to void may be due to a reflex spasm of the compressor urethralis muscle as the result of injury and clots may pass from a minor injury, the history of trauma, of hemorrhage from the meatus and of perineal hematoma associated with inability to void generally indicate rupture of the urethra. Catheterization under strictly aseptic conditions should be attempted. The treatment for incomplete rupture of the urethra still remains a controversial subject. Higgins is satisfied if a soft rubber catheter can be passed into the bladder and believes that perineal section, which has been recommended, should be avoided if possible. If infection supervenes or a catheter cannot be passed into the bladder, perineal section is necessary.

In cases of intrapelvic rupture, the urethra is torn in association with crushing injuries of the pelvis. The rupture usually occurs at the apex of the prostate gland, tearing it from the membranous urethra.

25. Higgins, C. C.: Rupture of the Urethra, Report of 12 Cases, Surg. Gynec. Obst. **50**:639 (March) 1930.

The differential diagnosis of this condition and rupture of the bladder may be difficult. If the bladder is distended and palpable, the rupture is below the vesical sphincter. Suprapubic cystotomy and drainage of the space of Retzius should be done as soon as possible. Perineal section is performed from forty-eight to seventy-two hours after preliminary cystotomy. The catheter is passed in a retrograde direction from the bladder to the perineum and then out through the meatus. This catheter acts as a splint holding the neck of the bladder in normal position until the cut ends of the urethra unite. The catheter is usually removed in from forty-eight to seventy-two hours. Instrumentation may safely be instituted from ten to sixteen days after operation. Further treatment should be based on urethroscopic study.

The mortality in cases of rupture of the urethra is low if treatment is given immediately. Stricture may result but, under judicious care, will respond to treatment.

TESTES

Tumors.—Barringer, Stewart and Spies [26] stated that the formerly grave prognosis in cases of tumor of the testes has materially improved with the advent of irradiation. With adequate irradiation certain types of highly malignant neoplasms may be completely controlled even though demonstrable retroperitoneal metastasis is present. The reaction of tumors of the testis and of the resulting metastatic growth to irradiation is known to be variable. In certain cases the primary tumors and the metastasis disappear precipitately and do not recur within a period of years. In other cases the primary tumors react with varying promptness and usually do not recur, whereas the metastatic growths react well and may completely disappear so far as palpation can show, but recur after an interval. Others are resistant to radiotherapy.

One hundred and fifty cases of neoplasms of the testis are reported, in the majority of which the primary tumor had been removed elsewhere and the patient was referred for treatment by irradiation. In certain instances the primary tumor was never removed, the diagnosis resting on the conformation of the tumor, the presence of palpable metastatic growths and the reaction to irradiation. In 42 of the 150 cases the testis was removed either before or after irradiation and the pathologic examination was made. If irradiation failed to control the tumors, analysis showed that the treatment had not been sufficient, and the dosage was practically doubled in such cases. When metastatic growths are enormous and the patient is in general poor health, sufficient treatment to control the tumors cannot be given.

26. Barringer, B. S.; Stewart, F. W., and Spies, J. W.: Testicular Neoplasms, Ann. Surg. **91**:115, 1930.

The advisability of removing primary tumors of the testis after irradiation is a controversial question. Barringer, Stewart and Spies perform orchidectomy as a routine: (1) in order to determine the type of tumor and to gain information as to the probable prognosis and the probable amount of irradiation necessary; (2) to obviate the necessity of subsequent overirradiation of the opposite testis, and (3) to prevent local recurrence in what may be an adult teratoma on the presumption that resumption of activity of more anaplastic portions may recur.

Of 113 patients who received treatment and were traced, 41 are living and clinically free from disease. Of the 113, the condition of 13 was primarily operable without palpable metastasis. Ten (79 per cent) are alive and clinically free from disease. The condition of 16 patients was primarily inoperable with demonstrable metastasis; 4 (25 per cent) are clinically well. Three patients in the operable group had recurrence; they (100 per cent) are all clinically well. Eighty-one patients had recurrent cases with inoperable local recurrences and inoperable metastatic lesions; 24 (30 per cent) are without evidence of disease.

[*Editorial Note.*—The variability in radiosensitivity of testicular neoplasms is well emphasized. The fact that sixteen patients with inoperable cases and three with recurrent cases were treated with 25 per cent clinical cure by radiotherapy argues well for this form of treatment if subsequent reports show these results to be consistent.

A few years ago, Hinman advised extensive radical resection of the regional lymphatic glands as a means of combating tumor of the testis. Young reported 50 per cent of one year cures in eight cases, and rather discouraged irradiation except as a postoperative measure. Probably, as the situation stands, orchidectomy and irradiation will usually give the best results.]

EPIDIDYMIS

Tuberculosis.—Cecil [27] described an operation for tuberculosis of the epididymis, the object of which is the clean removal of the epididymis and sinuses and the securing of primary healing. The tuberculous sinuses are painted with pure carbolic acid, after the scrotum has been cleansed. An elliptical incision is then made through the skin around the sinus. While the pressure above the testis is still maintained with the hand, light elliptical cuts are made concentrically, dividing bands of tissue directly down to the tunica vaginalis. These concentric cuts are kept close around the elliptical incision in the skin. As the cuts are made, the testis and epididymis begin to extrude from the scrotum. The scrotum is immediately wrapped with warm salt

27. Cecil, A. B.: An Operation for Tuberculosis of the Epididymis, Surg. Gynec. Obst. **50**:624 (March) 1930.

packs, covered with a towel and kept surgically clean. The tunica vaginalis is opened and the epididymis is separated from the testis. The epididymis and testis are both wrapped in warm salt packs and set aside. A clamp is pushed up along the vas deferens until it corresponds with the external ring. A small nick is made over the tip of this clamp and another clamp, which is used for clamping off the vas, is pushed down along the same path. The vas is cut between two clamps. The clamp and vas are then drawn upward to bring the vas out in the groin, but at no time is the clamp removed from the vas or is the vas ligated, as such attempts are likely to infect the wound. A single stitch is passed through the nick. This stitch passes through the outmost covering of the vas. The clamp, with the vas still fastened in it, is wrapped in gauze and strapped to the abdomen. The scrotum is pulled down over the testis and closed by interrupted dermal sutures. The wound is covered with collodion. The scrotum is supported with a binder. In about seven or eight days the vas comes away at the level of the skin.

URINARY LITHIASIS

Etiology.—Hinman, Charnock and Dart[28] considered some of the hypotheses concerning the etiology of urinary lithiasis which have been subjected to experimental study. Such etiologic agents are diet, mechanical or anatomic features, foreign bodies, infection or microorganisms and urinary colloids.

The problem of the formation of calculi in which the urinary solids are precipitated as fused, hard concretions rather than individual crystals is one of chemical precipitation. The basis of future knowledge of this problem seems to be in the field of colloidal chemistry. The process which can alter the action of the urinary colloids appears at this time to make up the foundation in the formation of urinary calculi.

In order to check the relation between the hydrogen ion concentration of the urine and the balance of the urinary colloids, a series of experiments was carried out to test the variation of crystalloid precipitation under different hydrogen ion concentrations of the urine. The factors of foreign body and infection were eliminated and stones formed within the pelves of experimental animals by oxamide. The oxamide is precipitated from the urine in such a way that the individual crystals tend to fuse. It was found that the urine of these rabbits were normally about p_H 7. Three classifications were made, alkaline and normal, and the animals were put on a diet which would keep the urine at a relatively

28. Hinman, F.; Charnock, D., and Dart, A. E.: Studies of the Etiology of Urinary Lithiasis, Proc. Ninth Meeting Clin. Soc. Genito-Urin. Surg., San Francisco, July, 1929.

wide variation of hydrogen ion concentration. The following points were noted: negative results without signs of concretions or oxamide deposits; fine sand visible macroscopically at necropsy and small concretions of sufficient size to cause urinary stasis when passed into the ureter. It was concluded that in rabbits having a strongly alkaline urine there is a tendency to the formation of stone.

[*Editorial Note.*—Keyser, in 1922, studied oxamide lithiasis in rabbits. The reaction of the urine of the rabbits, grossly controlled, seemed to affect little the deposition of oxamide in the urinary tract. Therefore, this report is somewhat in conflict.

Two points should be made. 1. Oxamide is a crystalloid foreign to the urinary tract of the animal. Therefore, conclusions drawn from a study of the formation of oxamide stones should not be applied directly as pertinent to the usual type of lithiasis seen in animal life. In other words, oxamide lithiasis is not a biologic process, but an unusual manifestation of chemical poisoning. However, the physical features of oxamide lithiasis, such as the fusing of the crystals, does seem to demonstrate the usual process in the formation of urinary calculi, as seen clinically. 2. From clinical evidence it seems fairly certain that the reaction of the urine does have some part in the formation of calculus. The calculi found in the lower animals, such as sheep and dogs, are almost consistently of the carbon variety and are associated with alkaline urine. In human beings phosphate calculi are most frequently associated with alkaline urine and with urea-splitting organisms of the proteus group. Oxalic and uric acid calculi are more often associated with urine of lower hydrogen ion concentration, but the ranges have not been accurately determined. Crowell has been able to stop the formation of cystine calculi in a patient by keeping the urine at a range of high alkalinity.

These features would tend to show that the reaction of the urine is of importance in the formation of stone, but in just what physicochemical manner this factor acts has not as yet been determined.]

Calculi in Infancy.—Campbell,[29] in reviewing a series of 30 cases of urinary calculi in infancy and childhood, observed that stones of later childhood are usually of urate or calcium phosphatic composition; from 10 to 15 per cent are composed of uric acid. Urinary calculi may appear at any age; they have been found in a 6 and in an 8 month old fetus. Urinary lithiasis is predominantly a disease occurring in boys: in a series of 2,000 cases reviewed, only 77 were girls. The ratio of incidence was 17 on the right side to 7 on the left. In about 10 per

29. Campbell, M. F.: Urinary Calculi in Infancy and Childhood, J. A. M. A. **94**:1753 (May 31) 1930.

cent the involvement was bilateral. Clinical observations show that the greatest obstacle to the passage of stones occurs at the vesical outlet, undoubtedly an explanation of the higher incidence in the male.

The symptoms of stone are chiefly those of infection of the urinary tract, although pain, whether due to urinary obstruction or to the presence of the foreign body, may be the first symptom apparent to the patient. Pyuria, urinary frequency and dysuria, together with localized, radiating or indistinct pain, are the most constant complaints. Stone without pyuria is rare. The amount of pus varies. A few scattered white blood cells to each high power field and thick, milky urine containing from 30 to 40 per cent of gross pus on standing may be noted. When the stone is renal or ureteral, the radiation of pain is usually toward the groin, pubis or isolateral genitalia. It may terminate in the lower abdominal quadrant. In extremely young patients, the passage of renal or ureteral stones generally causes symptoms similar to those of enteral colic; the pain is likely to be more continuous and not accompanied by diarrhea or other intestinal symptoms. Occasionally the passage of stones from the upper tract is manifested by acute symptoms of vesical calculus.

Laboratory examinations are important as the first step in a complete urologic examination. A roentgenogram is taken to ascertain the presence of stone, although the stones characteristic of early childhood are of uric acid composition and are not radiopaque. In older children from 10 to 15 per cent of urinary calculi will not cast a shadow in the roentgenogram. The treatment for urinary calculus in children is usually surgical, but in a few cases ureteral stones will pass following ureteral dilatation. About 90 per cent of all renal stones pass to the bladder and most of these eventally pass from the meatus. Nephrectomy is indicated only when the kidney is totally destroyed or the stone is so large that its removal by nephrotomy would probably result in ultimate destruction of the kidney. Removal of a stone by pyelotomy will often conserve the kidney. Impacted ureteral calculi are easily removed by ureterotomy. Although small soft stones of the bladder may be crushed by lithotripsy, large or hard stones are most successfully removed by cystotomy. The latter is the method of choice because any obstructions to the neck of the bladder may be destroyed through the open wound, or the diverticula may be resected.

UROGRAPHY

McCrea [30] called attention to the necessity of having a pyelographic medium that can be detected as it regurgitates from the ureter when

30. McCrea, L. E.: A Contrasting Medium for Pyelographic Study, J. A. M. A. **93**:987 (Sept. 28) 1929.

used in conjunction with indigo carmine. Sodium iodide, now the most universally used pyelographic medium, cannot be observed when the regurgitated fluid from the ureter is colored by indigo carmine. The following medium has been prepared and is now being successfully employed: sodium iodide, 12 Gm.; emulsion of silver iodide 5 per cent, 20 Gm.; distilled water sufficient to make 60 Gm. This combination is a thin, watery, creamy white mixture and can readily be detected by the observer watching the ureteral orifice as a bluish cream-colored fluid. The contrasting medium is of advantage in cases of obstruction of the ureter.

Raffo and his associates [31] stated that the combined method of cystoroentgenography was described by one of them for the first time in 1925, one year prior to the publication of the method of Resier.

Their technic is as follows: A catheter of large diameter is introduced into the bladder, the bladder is completely emptied, 30 cc. of barium sulphate in thick aqueous suspension is introduced, and then 100, 150 or 200 cc. of air or oxygen is injected until the patient complains of slight pain. Before the roentgenograms are taken, the patient is asked to turn once or twice so as to obtain a uniform coating of the vesical mucosa by the opaque medium. The roentgenograms are taken in the usual way. The lesions of the bladder appear either in the form of filling defects or as dense shadows.

The method of Resier, using iodized oil, does not always demonstrate the irregularities plainly because the higher viscosity of the iodized oil prevents its even distribution on the surface of the mucous membrane. Not infrequently roentgenograms are obtained which do not correspond to actual conditions.

Raffo and his associates have used the combined cystoroentgenography for three years with satisfactory results. Since the filling defects and increased opacities indicate only the site and extent of the lesion and do not indicate its true nature, the method should be used only in conjunction with other clinical procedures.

Haret and Frain [32] reported a case of multiple calculi of the bladder in a man, aged 40. At operation seventeen stones were found, twelve of which were about 2.5 by 2 cm. and five somewhat smaller. A cross-section of one of the larger stones revealed that the central portion of the calculus consisted of a blue-stained, oily substance which on chemical analysis was found to be gomenol stained with methylene blue (methylthionine chloride, U. S. P.). The bacteriologic examination revealed

31. Raffo, Vittorio; and Vallebona, Allessandro: Quelques remarques a propos de la cystoradiographie, J. de radiol. et d'électrol. **13**:481 (Sept.) 1929.

32. Haret and Frain, M.: Radiographie de la versie; une image rare, Bull. et mém. Soc. de radiol. méd. de France **17**:229, 1929.

the presence of active staphylococci. Many years previously gomenol had been injected into the bladder and at the same time methylene blue pills were given. It is probable that the air bubbles which formed at the time of the injection of the gomenol became stained with the methylene blue, and later stones formed. The presence of active staphylococci within the oily substance of the stones so many years later dissipates all illusions with regard to the antiseptic value of gomenol.

Trattner, Wright and Barlow [33] stated that the characteristic action of 12 per cent sodium iodide on the ureter consists in a marked increase of tonus, frequently to the degree of spasm which may be either regional or involve the entire organ. Relaxation of the ureter may also occur. In the interpretation of the pyelo-ureterogram, besides the normal anatomic constrictions and dilatations, and the effects of pressure from injection, it is essential to distinguish the functional response of the ureter produced by the sodium iodide solution from that of an organic lesion.

Bergerhoff [34] pointed out that the older method of pyelography in which the contrast medium was brought directly into the urinary passage was not physiologic. Another method has therefore been perfected by which a contrast medium that consists of a combination of urea and of iodine is injected into the cubital vein and is excreted through the urinary system. Not only does this contrast medium facilitate roentgenoscopy, but its elimination reveals the functional activity of the urinary system. Bergerhoff enumerated the cases in which this method of pyelography should be used and also the cases in which it is contraindicated. Following a description of the mechanism of the injection of the contrast medium and of the roentgenographic technic, he reported several cases that illustrate the great value of the method. He pointed out that this method of pyelography makes it possible for the physician who is not a specialist in urology to diagnose disorders of the urinary system, and consequently it enlarges the field of his activity. Indications for operative treatment can now be more precise than before this technic was perfected.

Béclère, Porcher and Henry [35] experimented with the preparation employed by von Lichtenberg for intravenous pyelography at St. Hedwig's Hospital in Berlin. This preparation consists of an iodized

33. Trattner, H. R.; Wright, H. B., and Barlow, O. W.: An Experimental Study of the Action of Sodium Iodide on Excised and Intact Ureters of Dogs, J. Urol. **23**:441 (April) 1930.

34. Bergerhoff, W.: Die Anwendung der intravenösen Pyelographie in der innern Medizin, Med. Klin. **26**:232 (Feb.) 1930.

35. Béclère, H.; Porcher, P., and Henry, Robert: Premiers resultats de la méthode de Lichtenberg. (Pyelo-uretero-cystographie par injection intra-veineuse), Bull. et mém. Soc. de radiol. méd. de France **18**:79, 1930.

substance derived from pyridine. It is made in the form of a water-soluble powder, it is absolutely nontoxic and its excretion begins within five minutes after the intravenous injection. The roentgenograms taken ten minutes after the injection are not sharp, but they demonstrate clearly the renal pelvis, the ureters and the bladder.

The method has two advantages: It permits of a study of the structure of the renal pelvis, ureters and bladder in all cases in which ureteral catheterization is impossible or contraindicated, and it gives information with regard to the intimate phenomena of urinary excretion.

The technic is as follows: Forty grams of the powder is dissolved in 80 cc. of double distilled water. After the addition of 20 cc. more of double distilled water, the solution is filtered through a regular filter paper or sterile gauze, is placed for twenty minutes in a water bath, is refiltered and is maintained at a temperature of 37 C. The intravenous injection is performed according to the usual technic (in the vein of the arm) except that after the injection of the first half of the solution (50 cc.) there is a three minute wait before the second half is injected.

The roentgenograms are taken fifteen minutes, thirty minutes and one hour and fifteen minutes after injection. The second roentgenogram, as a rule, shows the maximum contrast. In some of von Lichtenberg's cases positive roentgenograms were obtained six and even twenty-four hours after the injection.

Kielleuthner [36] has used an iodopyridine compound for intravenous pyelography for the last three months in a series of thirty-four cases. Roentgenograms were taken from ten to fifteen minutes and from twenty to forty minutes later; in case of disturbed renal function they were taken one hour, two hours and several hours later. All roentgenograms were satisfactory, and ill effects did not follow the injection. The method is of special value in cases in which direct pyelography is impracticable; for example, in cases of children, ureteral stones, malformations and certain abdominal tumors. It is contraindicated in bilateral conditions of the kidney and in thyrotoxicosis.

Roth and Wright [37] stated that the iodopyridine compound is neutral, is more than 50 per cent soluble in water and contains 42 per cent of iodine. It is an extremely stable chemical compound, and its opacity to roentgen rays is excellent.

Important information was obtained by comparing roentgenograms of a series of cases, and it is suggested that the use of serial changing casset holders in conjunction with a Potter-Bucky diaphragm might be of great advantage.

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36. Kielleuthner: Ueber eine neue, aussichtsreiche Untersuchungsmethode an den Harnorganen (Uroselektan), München. med. Wchnschr. **77**:276 (Feb.) 1930.

37. Roth, E. J. H., and Wright, H. W. S.: Intravenous Pyelography, Brit. M. J. **1**:778 (April 26) 1930.

Ill effects were not observed from the injection. There was a slight increase in the pulse rate and blood pressure and cramping of the anterior muscles of the shoulder in a few cases, but the symptoms always disappeared within fifteen minutes. The method is perfectly safe, even in cases in which there is marked decrease of renal function. The only contraindications are anuria, uremia and gross disease of the liver and kidney.

In Roth and Wright's series of sixty roentgenograms, they noted that the shadow of the left kidney appears slightly less dense than that of the right. They did not succeed, as others have done, in visualizing by roentgenograms the pelvic shadow accurately enough for pyeloscopy. On the roentgenograms, there was a satisfactory shadow after six minutes, and in fifteen minutes there was a perfectly clear outline of the whole of the urinary tract.

An iodopyridine compound can also be used as a test of renal function, since it is easily recovered from the urine. On the addition of hydrochloric acid, it forms a heavy white precipitate when the hydrogen ion concentration reaches from 2.8 to 3. Chemical estimation, however, is not always necessary because the specific gravity is a reliable guide of the drug present. It should reach between 1,045 and 1,050 within an hour.

Roth and Wright were able to confirm the experience of von Lichtenberg, according to which, although advanced noninfected hydronephrosis gives an excellent though perhaps delayed shadow, infected or congested pyonephrosis may not give a shadow.

In conclusion, the opinion is expressed that intravenous pyelography, by means of an iodopyridine compound, will play an important part in urologic diagnosis, since it is a reliable test of renal function and is a pyelographic contrast medium.

Hryntschak [38] since 1925, has experimented on animals with numerous opaque mediums for the visualization of the parenchyma and pelvis of the kidney. The following criteria were found to be of significance: (1) The opaque medium must be entirely harmless to the renal tissues; (2) it must be nontoxic; (3) it must possess sufficient contrast (iodine or bromide); (4) it must represent a stable preparation (so that iodine or bromide is not liberated in the organism); (5) it should be neutral, soluble in water (to at least 20 per cent) and permit of sterilization by boiling, and (6) it should be excreted in its entirety in the shortest possible time.

38. Hryntschak, Theodar: Studien zur röntgenologischen Darstellung von Nierenparenchym und Nürenbecken auf intravenösem Wege, Ztschr. f. Urol. **23**: 893, 1929.

The preparations used by Hryntschak were made synthetically. Simultaneously with the intravenous injection of the opaque medium, pituitary extract was administered intramuscularly in order to increase the power of concentration of the kidney, and atropine was given to decrease the peristalsis of the pelvis and the ureters. Good results were obtained, although the method needs further improvement.

The dose of opaque substance injected by Roseno [39] for intravenous pyelography is described briefly. The preparation is called "pyelognost" and is produced by Gehe and Company, Dresden. Sixty-three grams is injected into a normal patient weighing from 50 to 90 Kg.; 1.5 Gm. is subtracted for every kilogram of body weight under 50 Kg., and 1.5 Gm. is added for every kilogram of body weight over 90 Kg.

Roseno [40] gave the results of the clinical application of an iodopyridine compound in human beings as follows: Intravenous pyelography is of great advantage in all cases in which the usual pyelography by retrograde injection is contraindicated as, for example, in urethral stricture, atrophy and tuberculosis of the bladder, occlusion of one of the ureters and tuberculosis of one of the kidneys.

Normally the function of the kidney consists in excretion of the urine. This means that after the injection of the opaque medium the substance is excreted so fast that visualization by roentgenograms is not possible. In order to produce greater concentration of the iodine within the excreting kidney, Roseno added urea, which, in this particular instance, served two purposes: it forms a sort of carrier for the iodine, directing it toward the kidney, and it acts as a diuretic in increasing the permeability of the kidney filter.

The idiosyncrasy for iodine is tested (skin test) the day previous to the examination. If such idiosyncrasy is not present the solution (the nature and concentration are not described) is injected intravenously within from five to fifteen minutes. At the time of injection the bladder must be kept full so as to produce stasis in the renal pelvis; this delays the excretion of the opaque medium. Roentgenograms are taken immediately, three and five hours after the injection.

There is a sensation of pressure in the head and occasionally in the thorax associated with a feeling of faintness, such as is observed following the completion of the injection. A little later there is a sensation of thirst, sometimes necessitating the taking of fluids. In other instances there is evidence of headaches and slight elevation of temperature occasionally lasting for more than twenty-four hours. All symptoms disappear within forty-eight hours.

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39. Roseno, A.: Die intravenöse Pyelographie, Klin. Wchnschr. **8**:1623 (Aug. 27) 1929.

40. Roseno, A.: Die intravenöse Pyelographie, Klin. Wchnschr. **8**:1165 (June 18) 1929.

The normal pyelogram obtained after intravenous injection of the contrast medium is different from that obtained from the retrograde injection in that it appears smaller and less distorted. This, in Roseno's estimation, is due to the fact that mechanical distention is entirely absent in intravenous pyelography.

Twelve roentgenograms illustrate the value of intravenous pyelography in various pathologic conditions. In case of complete occlusion of one of the ureters by stone, kinking or tuberculous stricture, it is possible to obtain a good visualization of the kidney and a portion of the ureter above the stricture. In stenosis underneath the ureteral ostia (urethral stricture and hypertrophy of the prostate gland) good visualization of the urinary tract is obtained because of the stasis produced by the stenosis. In cases of stones of the kidney and ureter, one may localize exactly the site of the stones and also the type and extent of the stasis proximal to the stone, and obtain at the same time much information concerning the function of the diseased kidney and the opposite normal kidney. In anomalies of the uropoietic system the type and extent of the anomaly of the complications resulting therefrom can easily be determined. In tuberculosis of the kidney, besides impaired "reflektorische" excretion, tuberculous cavities in the region of the calices and parenchyma may be demonstrated.

In cases of renal tumor as well as of renal cyst, the retrograde pyelography is of greater advantage. Intravenous pyelography, because of almost complete loss of excretion, leads here only to poor visualization of the urinary tract. Most of the so-called functional ureteral kinkings and Hunner's ureteral strictures are artefacts, produced probably by manipulation during retrograde pyelography.

Von Lichtenberg and Swick [41] took a pessimistic point of view in a recent consideration of Roseno's work on the value of intravenous pyelography. By this they did not mean to underestimate the idea of intravenous pyelography, but to express doubt that a suitable medium for injection would be found. Yet Roseno, by emphasizing the physiologic and pathophysiologic phenomena, obtained marked results in this respect.

In comparing intravenous pyelography by means of iodopyridine compound with retrograde pyelography, the authors attempted to determine at the St. Hedwig Krankenhaus, aided by Rave, roentgenologist, how far the two methods agreed and what practical conclusions could be drawn. Of the eighty-four cases studied, thirty-five were later checked at operation and one at postmortem examination.

In all instances a good visibility of the urinary tract by the roentgen ray was obtained. If a shadow of the kidney was not demonstrable,

41. von Lichtenberg, A., and Swick, M.: Klinische Prüfung des Uroselectans, Klin. Wchnschr. 8:2089 (Nov. 5) 1929.

the kidney either was not present, or function was greatly or entirely destroyed. The functional disturbances of the urinary tract could also be studied with great accuracy.

In the 84 cases studied (this number later increased to 160), satisfactory information was obtained concerning the best therapeutic procedure from intravenous pyelography alone in 75 per cent; in the remainder of the cases the examination had to be supplemented by cystoscopy, catheterization of the ureters and pyelography. The functional test as estimated from observations by the roentgen rays likewise led to positive information in 75 per cent of the cases.

Intravenous pyelography is indicated: (1) in all instances in which cystoscopy, ureteral catheterization and direct pyelography are contraindicated either for anatomic, pathologic or technical reasons; (2) in all cases of ureteral occlusion, and (3) in all cases in which the application of direct pyelography is associated with certain risk to the patient.

In the cases of limited renal function direct pyelography by the routine procedure, on account of the better contrast, leads to more satisfactory results.

Since 95 per cent of the injected iodine is excreted in the urine within from six to eight hours, it was attempted to find whether the rate and the percentage of the iodine excreted could not be used as a basis of the functional test of the uropoietic system. Three methods were employed for this purpose: (1) the determination of the excreted iodine; (2) the quantitative determination of the excreted iodopyridine compound, and (3) the determination of the specific gravity of the urine, this increasing proportionately with the amount of iodine present. So far it has not been possible to find out which of the three methods would be of practical value.

The association of pyelography with pyeloscopy is indicated also in the intravenous application of the method.

An attempt was made to administer the iodopyridine compound by mouth, but this procedure proved unsatisfactory.

Swick,[42] after a brief description of the procedures which led to the discovery of an iodopyridine compound by Binz and Räth, defined the characteristics of this compound as follows: The iodopyridine compound is nontoxic, soluble in water and neutral in its reaction, and under normal conditions it is excreted as such through the genitourinary tract within eight hours practically to the extent of from 90 to 100 per cent. The iodine in the molecule exists in a stable, organically bound state, thus explaining why iodism has never been observed. Its

42. Swick, M.: Intravenous Urography by Means of Uroselectan, Am. J. Surg. 8:405 (Feb.) 1930.

tolerance is exceedingly great; theoretically 180 Gm. of the substance, in terms of iodine 75.6 Gm., can be administered to a person weighing 60 Kg.

A child aged 7 years would receive half the dose and a child aged 2 years a fourth of the dose administered to an adult. The injection is made in two stages, at intervals of from three to five minutes, by using from five to six syringes previously sterilized in distilled water. The first roentgenogram is made fifteen minutes after the last injection, the second about from twenty to thirty minutes after the first roentgenogram and the third a corresponding period after the second roentgenogram. In disturbances of renal function, subsequent films are taken at intervals of from two to four hours.

The reaction consists of thirst and generalized warmth, particularly of the face and region of the bladder, and occasionally of nausea. Shivering and vomiting of short duration occurred in a case of nephrosis. A child aged 10 years died shortly after the injection, but the uremia that had existed a long time previous to the injection was probably responsible.

Intravenous urography is indicated whenever ureteral catheterization is dangerous or mechanically impossible, in cases of infection of the lower part of the genito-urinary tract, in the presence of bleeding, in cases of implanted ureters and in the case of children.

Truchot [43] described four cases in which the application of intravenous pyelography led to the correct diagnosis. He used an iodopyridine compound for intravenous pyelography in about twenty examinations of the urinary system. The method of injection was that employed by von Lichtenberg. Ill effects were not observed except for a slight sensation of heat in the head lasting for a period of from ten to fifteen minutes.

The intensity of the shadow of the urinary tract was controlled roentgenoscopically, and roentgenograms were taken at the peak of the visibility of the image.

Ravasini and Gortan [44] have used an iodopyridine compound in ten cases in which the lesions were varied, such as mobile kidney, marked chronic cystitis, bilateral cystopyelitis in pregnancy, bilateral pyelonephrosis, stone in the pelvis of the kidney, double ureters, infected prostate gland, cystopyelitis in pregnancy, nine month pregnancy with constricted pelvis of the kidney and polycystic kidneys. The conclusion

43. Truchot: Presentation de quelques radiographies du systeme urinaire, obtenues après injection intra-veineuse d'uroselectan, Bull. et mém. Soc. de radiol. méd. de France **18**:171, 1930.

44. Ravasini and Gortan: Il quadro radiografico delle vie urinaire mediante l'iniezione endovenosa con l'uroselectan, Radiol. med. **17**:327 (March) 1930.

is reached that the preparation is entirely innocuous; in two cases there was temporary elevation of temperature but this was due, as already suspected by von Lichtenberg, to the distilled water. Good roentgenograms of the urinary tract were obtained in all cases in which the renal function permitted sufficient elimination of the opaque salt. The method is indicated in all cases in which pyelography cannot be performed. It also gives certain information of a physiologic character.

Vallery-Radot and his associates [45] stated that Osborne, Sutherland, Scholl and Rowntree, in 1923, used sodium iodide orally and intraveneously for the demonstration of the urinary tract roentgenologically. Volkmann, in 1924, after experimenting with lithium iodide, sodium bromide and sodium iodide, arrived at the conclusion that sodium iodide is the most suitable of the three. Von Lichtenberg, in 1924, Lenarduzze and Pecco, in 1927, and Roseno, in 1929, made further contributions to this subject. The method of Roseno consisted of intravenous injection of sodium iodide in association with urea, the latter acting as a diuretic and thus producing more rapid elimination of the iodine. Roentgenograms were taken within fifteen minutes, three hours and five hours after the injection.

Recently, von Lichtenberg and Swick contributed to the method of Osborne and his associates in introducing an iodopyridine compound. This product, prepared by Binz and Räth, consists of a sodium salt of pyridine with 42 per cent iodide organically fixed. The injection is made in two stages, at intervals of three minutes. The roentgenograms are taken fifteen minutes, forty-five minutes and one hour and fifteen minutes, or in the event of functional disturbance of the kidney, six hours, twenty-four hours and even thirty-six hours after the injection of the opaque medium.

Vallery-Radot and his associates investigated the value of the method of von Lichtenberg and Swick by injecting the iodopyridine compound intravenously into two rabbits and one guinea-pig. The preparation was well tolerated, the maximum tolerance dose being 7 Gm. for each kilogram of body weight in rabbits, thus giving a maximum dose of 180 Gm. for a human being weighing 60 Kg.

As a result of these experiments on animals, the iodopyridine compound (40 Gm. dissolved in 100 cc. double distilled water) was injected also into one human being, and roentgenograms were taken one, six, sixteen, twenty-three, forty-one and fifty-seven minutes and one hour and thirty-three minutes after the injection.

It was concluded that the method of von Lichtenberg and Swick leads to good visualization of the calices, pelvis of the kidney, ureters

45. Vallery-Radot, Pasteur; Dalsace, Jean; Nemours-Auguste, and Dérot, Maurice: Nouveau procédé d'exploration radiologique des voies urinaries, Presse méd. **38**:385 (March 19) 1930.

and bladder. It also permits the evaluation of functional disturbances of the kidney. The method marks real progress in the study of renal lesions.

Lotsy [46] stated that the irritation caused by the continuous accumulation of eggs of *Bilharzia* in the submucosa of the bladder, kidney and colon leads to a large round cell infiltration of the contiguous tissues, resulting later in mucous papillomas of various forms. After the lapse of one year the eggs become calcified. He presented numerous cases illustrating the different roentgenologic aspects of papillomas and calcification in bilharziasis of the urinary tract.

The following difficulties are especially emphasized from the point of view of differential diagnosis: (1) possible confusion with calculi of the bladder, ureter and kidney; (2) possible confusion with papillomas or infiltrations of the intestinal tract which project into the region of the bladder, ureter or kidney, and (3) misjudgment of the papillomas and calcifications of the urinary tract in cases in which elongation and tortuosity of the ureters are present.

Definite diagnosis was obtained in most cases by the simple use of compression, evacuation of the bladder and roentgenograms in different views. Lotsy is convinced that the injection of opaque solutions for the purpose of differential diagnosis, as advocated by others, is not necessary.

Sargent [47] reviewed a series of vesiculograms showing about 200 seminal vesicles, and compared them with the clinical data. The series included normal, as well as acute and chronic, cases of gonorrheal vesiculitis and tuberculous vesiculitis. He concluded that the vesiculogram is constant and does not vary in normal men, nor does it vary from time to time in the same subject as long as the condition of the vesicle remains the same. Partial or total dilatation of the seminal vesicle occurs commonly in cases of chronic vesiculitis of several months' duration. This dilatation is thought to be atonic in nature and is not permanent if the inflammation subsides. Dilatation of the ampulla of the vas deferens or of the ejaculatory duct occurs as the result of organic stricture, and, when present to any degree, remains permanently. Diminution in the cavity of the vesicle is a constant observation in acute gonorrheal epididymovesiculitis, and is thought to be due to inflammatory swelling of the vesical wall. It is temporary and disappears with recovery from the disease. Contraction of the wall of the

46. Lotsy, G. O.: Sur les difficultés causées par la bilharziose dans l'examen radiographique des voriés urinaires, Bull. et mém. Soc. de radiol. méd. de France **17**:232 (July) 1929.

47. Sargent, J. C.: Interpretation of the Seminal Vesiculogram, Radiology **12**: 472 (June) 1929.

vesicle, with extreme decrease of the cavity, even to the point of obliteration, occurs as the result of long-standing inflammation, a change that is observed in the vesiculogram in chronic vesiculitis, either of gonorrheal or of tuberculous origin. The vesiculogram reveals abscess of the seminal vesicle, when present, and communication with its cavity. Obstructions of the seminal tract, as well as anomalies of the vas and seminal vesicle, are revealed in the vesiculogram.

ANOMALIES

Hurt [48] studied at necropsy fifty-one male and fifty female infants. Sixty-three were stillborn; the remainder lived for periods of from a few minutes to twelve days. Anomalies of the urinary tract were observed in five cases. In one case bilateral polycystic kidneys were present; the right kidney weighed 15 Gm. and the left kidney, 12 Gm. Both were completely cystic, and the pelves were small. In the second case the cause of death was intracranial hemorrhage and prematurity. There was partial stricture of the left ureter 1 cm. above the ureterovesical juncture. Mild degrees of hydro-ureter and hydronephrosis were present. The left ureter was 5 mm. in diameter, and the right, 2 mm. There was definite narrowing of the left ureter about 2 cm. below the kidney. Each kidney weighed 6 Gm. In the third infant both kidneys were polycystic, and there was complete stricture of each ureter just below the kidneys. The ureters were patent from the strictures to the bladder, but were delicate and thin-walled. The right kidney weighed 4.2 Gm. and the left, 4.7 Gm. The fourth case was that of a stillborn, premature male infant. The urinary anomaly in this case was such as to be incompatible with continuance of life for any length of time. The right kidney and ureter were absent. The left kidney weighed only 2 Gm. and appeared to be a fibrous mass; a pelvis was not demonstrable. The left ureter was small and delicate; it was obliterated just below the kidney but was patent from the point of obliteration to the bladder. In the fifth case the patient was a premature girl, aged 10 days. The cause of death was a defect in the interventricular septum. There was almost complete stricture of the left ureter just below the renal pelvis, with marked left hydronephrosis. The pelvis was about five times normal size, and the cortex was considerably thinned. The left kidney weighed 16.3 Gm. and the right, 10.2 Gm.

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48. Hurt, A. S.: Anomalies of the Urinary Tract in Infants, Am. J. Dis. Child. **38**:1202 (Dec.) 1929.

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EXPLORATION OF THE PERICARDIUM AND DECOMPRESSION OF THE HEART

REPORT OF CASES

WYMAN WHITTEMORE, M.D.
BOSTON

The transactions of this society contain few articles devoted to surgical treatment of the heart. Because it is not given to any one surgeon to have many of these cases, it is important for members of this society to report such cases in order that a considerable number of cases may be grouped collectively for individual study. Following this idea, it is my desire briefly to report two cases.

REPORT OF CASES

CASE 1.—A man, aged 22, entered the Beth Israel Hospital, Boston, on Jan. 7, 1929. A week previously he had been struck on the left side of the chest by an automobile, and within three or four days pneumonia developed in the left lung.

On entrance to the hospital the temperature was 104 F.; pulse rate, 120; respirations, 30, and blood pressure, 112 systolic and 56 diastolic. The sputum contained type IV pneumococci. Examination of the blood showed: 5,230,000 red corpuscles; 16,000 white corpuscles, and 97 per cent polymorphonuclears. At the end of ten days, the temperature, which had gradually come down to 99 F., began to rise again, and signs of fluid developed in the left side of the lower part of the back. Aspiration thirteen days after entrance obtained pus with pneumococci which proved to be type IV. The empyema was drained the same day, and a section of the eighth rib was removed under local anesthesia. Three days later, the temperature was normal, but the following day it rose to 101 F. with a faint pericardial rub. Two days later the patient was seen by a medical consultant, who found definite pericardial friction rub, and expressed the belief that suppurative pericarditis would develop. Ten days after operation, roentgenograms of the chest showed: "a small amount of fluid present in the left side. There was a triangular area of increased density which merged with the right border of the heart, but did not obliterate it. The lung field was clear. The possibility of pericardial effusion could not be ruled out." Three days later, roentgenograms showed: "cardiac shadow as of water-bottle shape with the characteristic appearance of a large pericardial effusion." The following day the pericardium was aspirated on both the left and the right side, but nothing was obtained. Four days later, seventeen days after the operation, a roentgenogram showed the cardiac shadow slightly larger than before. The patient seemed to be losing ground gradually with considerable abdominal distress. The abdomen was distended, and vomiting occurred two or three times each day.

It was decided that exploration of the pericardium was justified in spite of the fact that nothing had been obtained by aspiration. On February 18, nineteen days after the operation for empyema, under local anesthesia, a section of the fourth costal cartilage on the left was removed; the pericardium was opened,

and a considerable amount of thin fluid was obtained. It was felt that there was probably a pocket of frank pus somewhere in the pericardium, and so the patient was given ether and a section of the fifth costal cartilage was removed. The opening into the pericardial cavity was enlarged and the pericardium explored. There were many adhesions, both anteriorly and posteriorly, between the heart and the pericardium. Some of these were broken up, and a cavity posterior to the heart containing considerable thin, slightly bloody fluid was opened into. This posterior cavity was drained with a small rubber catheter and the anterior cavity with a cigaret wick. Culture from the fluid contained pneumococci.

The day after the operation the patient's temperature was normal; the respiratory rate was 20 and the pulse rate, 90; all abdominal symptoms had disappeared. His temperature remained normal for the rest of his stay in the hospital, and he was discharged on March 10, thirty-nine days after the operation for empyema, and twenty days after the operation on the pericardium, with both empyema and pericarditis healed.

Three days before discharge, roentgenograms showed dulness in the left part of the chest, the result of a thickened pleura. There was no evidence of fluid. The left side of the heart appeared to be somewhat enlarged, but there was no evidence of pericardial effusion.

Three months after leaving the hospital the patient was allowed to return to work; he has been working steadily since then, and is in normal health.

My reason for reporting this case is that the operation was done in spite of the failure to obtain anything by aspiration of the pericardium. For years thoracic surgeons have been accustomed to explore the pleural cavity when there is good reason to do so, and there is no reason why the pericardial cavity should not be explored with just as much safety as the pleural cavity when there are indications to justify it.

The second case is one of a greatly enlarged heart due to valvular disease, in which it was hoped that cardiolysis would be of benefit.

Case 2.—An American schoolboy, aged 15, entered the Massachusetts General Hospital on Jan. 3, 1930, complaining of weakness and shortness of breath, which had been gradually increasing for the past seven months. There was no history of rheumatic fever or chorea. At the age of 5 he had had measles followed by repeated earaches and a discharging right ear. The ear condition appeared to be cured after tonsillectomy one year later. There had been no subsequent sore throats.

Seven months previous to entrance, a few days after a fall from which he had apparently suffered no ill effects, he noticed a swelling of the feet, ankles and legs while trying on shoes. An hour or so later he became exhausted, and collapsed on arriving home. He remained in bed five weeks, and then resumed activity gradually during three more weeks. At the end of this time he attended a summer camp for one month, where he exercised vigorously in spite of not feeling well. Four months before entrance his feet began to swell again, and he had some shortness of breath and palpitation after being up all day. He was in bed for the next two months, and then attended school for the following month. He did fairly well until one month before coming to the hospital, when he caught a cold, and a nonproductive cough developed, which has continued to the time of writing. Three weeks before I first saw him his face had begun to swell so much that he was unable to open his eyes in the morning. His legs

swelled to his knees if he was on his feet too long, and he became dyspneic on slight exertion. Two weeks before, he began to vomit, and he had vomited nearly everything eaten since.

Physical examination on admission showed a fairly well developed and nourished boy lying flat in bed. There was no pain; the breathing was rapid, and the face was puffy and flushed. The heart was enormously enlarged. There were systolic and diastolic thrills, with presystolic, systolic and rumbling diastolic murmurs of the apex and to and fro murmurs at the base. There was no second sound in the aortic area, but distinct and somewhat accentuated sounds at the pulmonic area. There was marked pulsation in the neck. The blood pressure was 120 systolic and 80 diastolic. The abdomen was tense and distended with some gas and a considerable amount of fluid. There was no edema at the ankles or sacrum.

Laboratory examination on admission showed that the urine was normal. The red blood count was 5,200,000; the white blood count, 19,000. A smear showed: polymorphonuclears, 55 per cent; lymphocytes, 36 per cent, without abnormality of any of the cells; the platelets were normal. The stool was normal. The Hinton test gave negative results. The liver function test (brown sulphthaleine) showed from 5 to 10 per cent retention after thirty minutes.

On admission the diagnosis was rheumatic heart disease with pericarditis, possibly adhesive. A roentgenogram of the heart taken at a distance of 7 feet showed "enlargement in all diameters, with the curves of the pulmonary conus and auricles particularly prominent."

An electrocardiogram taken on January 6 showed: normal rhythm, rate 100; a tendency to right axis deviation; low voltage: $Q.R.S._1$, —38-3; $Q.R.S._2$, —4. On January 7, the cardiac consultant gave the opinion that "anasarca with ascites at the age of 15 with evidence of cardiac disease makes the diagnosis of chronic pericarditis involving the mediastinum almost certain." He found involvement of the mitral valve with regurgitation. The size of the heart and electrocardiographic observations also favored a diagnosis of adherent pericardium, presumably rheumatic. He advised the use of digitalis, and mersalyl, 1 cc. every three days. The prognosis at that time was poor.

The following day the cardiac consultant said that the condition was "active and chronic heart disease with mitral involvement and undoubtedly chronic pericarditis." He expressed the belief that cardiolysis should be seriously considered. The same day roentgenograms showed no evidence of fluid in the pericardium.

For the following ten days the patient had a widely swinging temperature as high as 103 F., with a leukocytosis of from 12,000 to 20,000. Digitalis was given, 1½ grains (0.09 Gm.) daily, a total of 15 grains (0.97 Gm.). Between January 4 and 14 he received 60 grains (3.9 Gm.) of ammonium chloride daily. From January 5 to February 7, nine doses of mersalyl, either 1 or 2 cc., were given intravenously. On January 10, slight tenderness developed in two joints. Salicylates, 40 grains (2.6 Gm.) daily, were given between January 10 and 27. Four blood cultures between January 8 and February 2 were negative. During the first nine days, the generalized edema decreased markedly, owing to brisk diuresis. The patient showed a loss of 25 pounds (11.3 Kg.). No evidence of active endocarditis was found, except as suggested by the fever and leukocytosis. By January 23, the patient had regained 11 pounds (5 Kg.) and ascites had been increased. Mersalyl at this time is recorded as having caused an excellent diuresis.

On January 24, consultation was held. Cardiolysis was considered indicated, but was postponed for two or three weeks more of rest, administration of digitalis and diuretics in the hope that the infection and decompensation would subside.

For the next ten days, edema increased with little or no alleviation by diuretics, and cardiac embarrassment became more marked. The temperature fluctuated between 98.6 and 100 F.

Roentgenograms taken on January 31 showed the heart shadow somewhat increased in diameter across the auricles, with evidence of fluid in the pericardium.

On February 7, in a second consultation it was concluded that the recent increase in unfavorable symptoms and signs warranted operative intervention. This was defined to mean rib resection, with evacuation of pericardial fluid if present, and excision or section of the pericardium if adhesions or a fibrinous pericarditis was found. It was felt that the increase in stasis of the head and the upper extremities, combined with the small paradoxic pulse, favored the diagnosis of pericardial effusion with compression of the great vessels.

The patient was prepared for operation by continued administrations of digitalis, mersalyl and morphine. On February 8, an operation was performed. This was begun under local anesthesia, but within a few minutes the patient became very nervous, and it seemed wise to change to light ether anesthesia. The sternal ends of the third, fourth and fifth ribs were resected, and the portion of the sternum overlying the pericardium was removed. During this procedure it was reported that the blood pressure could not be obtained, but as soon as the bony structures overlying the pericardium were removed it was noted that the heart beat was much stronger, and at this time the blood pressure was reported as 120 systolic and 80 diastolic. This was encouraging. The pericardium was found adherent to the anterior part of the thoracic wall, but when opened, contained no fluid. A portion of the pericardium about 1½ inches (3.7 cm.) square was excised. Exploration of the pericardial cavity revealed dense adhesions between the heart and pericardium around the apex and along the left border. The defect in the thoracic wall was closed by muscle, fascia and skin. The patient stood the procedure well; on return to the ward, the blood pressure was 120 systolic and 80 diastolic. This dropped somewhat but rose to the same height within four hours after operation. Although slightly dyspneic, the patient was fairly comfortable.

The following morning the patient was sitting up in bed reading the newspaper, and declared that he felt very much better. Edema of the upper extremities and face had completely subsided, making it difficult to recognize the boy, although the swelling in his legs remained. The temperature was 101 F., but it came down to normal during the next five days. On February 14, six days after operation, he was seen by a heart consultant who said that there was slight improvement following the operation, with a fuller pulse, increased blood pressure and less edema of the face. The dependent edema and dyspnea had not changed appreciably. He said that the use of digitalis should be continued, 1½ grains being administered daily, with more diuretics. Two cubic centimeters of mersalyl administered intravenously might help to make more evident any improvement resulting from the operation. After five days his condition gradually changed for the worse. The temperature remained at 101 F.; edema of the lower extremities increased. Because of nausea and vomiting, the daily doses of digitalis were omitted. The urinary output following the administration of mersalyl increased from 20 to 40 ounces (567 to 1,134 Gm.). There was no appreciable diminution of edema. From February 15 to 17, the patient grew rapidly worse; dyspnea increased; tracheal râles developed and were audible at a distance. On February 17, the blood pressure dropped to 70 systolic and 40 diastolic; edema increased, and the patient was semicomatose. Epinephrine, caffeine and sodium benzoate

were given intravenously. The pulse became stronger. Three hours later the patient died before stimulants could be given. Unfortunately, there was no autopsy.

This case did not show the classic signs of adherent pericarditis, such as retraction with each systole and Broadbent's sign, nor was there a bulging of the pericardial region due to the great size of the heart.

Before undertaking the operation there were great doubts as to the value of cardiolysis in cases of enlargement of the heart, but it was felt that if there was adherent pericarditis associated with hypertrophy of the heart, and if at operation some of the adherent pericardium could be removed in addition to the excision of the ribs and sternum overyling it, there was a possibility of improvement. There can be no question but that there was temporary improvement, the improvement, however, lasting only four or five days. Disappearance of the edema of the face and upper extremities twenty-four hours after operation was encouraging, but although it is always unfair to draw conclusions from an isolated case, it would still seem doubtful whether the operation of cardiolysis is of sufficient value in cases of enlargement of the heart to justify its use in these desperate situations.

COMMENT

I have chosen these two cases because I believe that progress in thoracic surgery depends to a large extent on the sharing of failures as well as of successes, for only in reporting and comparing various experiences in this little known field can one form any real estimate of the lasting significance of any new surgical undertaking.

PERICARDIECTOMY IN THE TREATMENT OF THE PICK SYNDROME

EXPERIMENTAL AND CLINICAL OBSERVATIONS *

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AND
R. A. GRISWOLD, M.D.
CLEVELAND

INTRODUCTION

With the advent of asepsis, surgery emerged from the doldrums, where it had stood for centuries, and entered a period of unprecedented activity and advancement. A new era, that of operative development, had suddenly dawned. With bountiful promise for every new endeavor, surgery advanced from the beginning to almost the end of that great period in a mere half century. Within the short span of a surgeon's life this historic development could have been seen in panoramic view. Perfected and diversified as this development has been, surgery of the central circulatory system, of the heart with its pericardium, has not kept pace with the advancement in other fields.

The foundation for the development of cardiopericardial surgery has not yet been completely assembled.[1] This last great "Northwest of Surgery" stands today in a position scarcely more favorable than that occupied by abdominal surgery when the great Mikulicz advocated exploratory laparotomy for obscure abdominal conditions. The idea of exploratory pericardiotomy is greeted, even by surgeons of extensive experience, with surprise and spontaneous disfavor. Physicians, in general, do not believe that removal of the pericardium is worth while in the treatment for the Pick syndrome. Their objections, *a priori*, are: 1. The difficulties of the operation give to it a special hazard. 2. After the adhesions have been separated and the pericardium has

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1. Although surgeons have repeatedly opened the pericardial cavity to atmospheric pressure, the effect of pneumopericardium on the mechanics of the circulation has just recently been studied (Beck, C. S., and Cox, W. V.: The Effect of Pericardiostomy on the Mechanics of the Circulation, Arch. Surg. **21**:1023 [Dec. Part I] 1930). Although a number of surgical attempts to relieve stenosis of cardiac valves have been made, the physiologic basis for this work is yet to be elucidated. So far as we are aware, determinations of intrapericardial pressure in health or disease, in man or in laboratory animals, are yet to be taken. The first patient ductus arteriosus is yet to be ligated.

been removed, adhesions between the heart and its surrounding structures will surely reform. 3. The fibrosis extends into the cardiac muscle and a simple peeling off and removal of the pericardium would not be followed by a permanent improvement. Add to these objections the uncertainties of diagnosis, and the reluctance of physicians to accept this operation can be accounted for.

Pericardiectomy in the treatment for the Pick syndrome is followed by results nothing short of brilliant. What a pity that the diagnosis is so difficult and so infrequently made clinically! Because of the uncertain recognition of this condition, we champion diagnostic pericardiotomy in selected cases of circulatory failure of obscure cause.

Our investigations on the subject of adhesive pericarditis have been both experimental and clinical. Beginning with the primary purpose of producing the Pick syndrome experimentally and relieving it subsequently by operation, the work as it progressed took on a number of illuminating and, we believe, important aspects.

In this paper the discussion is confined entirely to the condition variously designated as concretio pericardii, synechia pericardii, symphysis cardiaca, pericarditis chronica adhaesiva and callous pericarditis. The term adhesive pericarditis is not always applicable to the condition under discussion. The clinical syndrome described by Pick may occur, as shown by our experiments, without the formation of adhesions between the heart and the pericardium; also, the presence of generalized intrapericardial adhesions is not necessarily associated with the Pick syndrome. The essential feature of the condition is a compression effect exerted on the heart by the contraction of scar tissue. We shall refer to the clinical description of this condition by the term "Pick's syndrome," without reference to the various factors that may have produced the compression effect on the heart.

Conditions in which adhesions exist between the external aspect of the pericardium and its contiguous structures are not discussed in this paper.

A résumé of the literature is given in the excellent articles by Schmieden [2] and Churchill.[3]

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2. Schmieden, V.: Ueber die Exstirpation des Herzbeutels, Zentralbl. f. Chir. **1**:46, 1924; Die Heilung der schrumpfenden Pericardial-Synechie durch Exstirpation des Herzbeutels, Acta chir. Scandinav. **57**:268, 1924; Neue Ergebnisse bei der Exstirpation des Herzbeutels, Arch. f. klin. Chir. **138**:552, 1925; Technique of Cardiolysis, Surg. Gynec. Obst. **43**:89-93, 1926. Volhard and Schmieden: Ueber Erkennung und Behandlung der Umklammerung des Herzens durch schielige Perikarditis, Klin. Wchnschr. **2**:5, 1923.

3. Churchill, E. D.: Decortication of the Heart (Delorme) for Adhesive Pericarditis, Arch. Surg. **19**:1457 (Dec.) 1929.

THE PICK SYNDROME PRODUCED EXPERIMENTALLY

Adhesions between the heart and the pericardium can be produced readily by the application of chemical irritants or by mechanical trauma to the epicardium or to the parietal pericardium. These procedures have not resulted in any circulatory disability that is demonstrable clinically. The adhesions produced by these methods consist of bands of fibrous tissue extending from one surface to the other usually without completely obliterating the pericardial cavity and without producing any thickening of the parietal pericardium itself.[4] In a study of the effect of surgical solution of chlorinated soda (Dakin's solution) in the normal pericardial cavity of the dog it was found that the solution produced a profound reaction.[5] This consisted of hemorrhage caused by the erosion of small blood vessels, as the immediate reaction, and of generalized adhesive pericarditis, sometimes with the development of polyserositis, as a delayed reaction. Death uniformly followed the development of polyserositis. The syndrome of adhesive pericarditis and polyserositis produced by the application of surgical solution of chlorinated soda in the normal pericardial cavity of dogs was exactly similar to the condition described by Pick[6] in 1896, which bears the name of Pick's disease.

The dog was anesthetized by ether or by sodium iso-amylethyl barbiturate injected intravenously. Mechanical respiration was provided by the Erlanger apparatus through an intratracheal tube. A short segment of the left fifth rib was resected subperiosteally and the thorax was opened. Either the solution of chlorinated soda was introduced into the pericardial cavity through an aspirating needle, or the pericardial cavity was opened and irrigated through a catheter. Usually from 50 to 100 cc. of the solution was used and this was applied for a period of from fifteen to twenty-five minutes. As soon as the irritant was introduced, the pulse rate became rapid and after a few minutes the fluid became hemorrhagic. A small opening was usually left in the pericardium so that fluid, as it formed, could escape and thus prevent the development of cardiac tamponade. The air was expelled from the pleural cavity and the wound was sutured in layers with silk.

During the postoperative period the dogs were examined at frequent intervals. The size of the cardiac shadow was determined by roentgenograms, which were taken at constant distances so that fairly accurate comparisons could be made. Venous pressures were determined by the direct method of inserting into the jugular vein an aspirating needle connected to an upright manometer and determining the height of a column of physiologic solution of sodium chloride sup-

4. Beck, C. S., and Moore, R. L.: The Significance of the Pericardium in Relation to Surgery of the Heart, Arch. Surg. **11**:550 (Oct.) 1925.

5. Beck, C. S.: The Effect of Surgical Solution of Chlorinated Soda (Dakin's Solution) in the Pericardial Cavity, Arch. Surg. **18**:1659 (April) 1929.

6. Pick, Friedel: Ueber chronische, unter dem Bilde der Lebercirrhose verlaufende Pericarditis (pericarditische Pseudolebercirrhose) nebst Bemerkungen über die Zuckergussleber (Curschmann), Ztschr. f. klin. Med. **29**:385, 1896.

ported in the tube.[7] Minute volume output determinations of the heart were made by means of the Fick principle. Electrocardiograms were taken with the dog in various positions to show the presence or absence of the shift of the electrical axis of the heart. The formation of fluid in the chest, abdomen and subcutaneous tissues was noted, as was also the weight, the circumference of the abdomen, the respiratory rate, the pulse rate and the condition in general.

Polyserositis did not always develop after this procedure. In some experiments, especially in those in which a small quantity of the solution was introduced, only a mild reaction followed. In other experiments, in which the solution was introduced slowly and over a relatively long period of time, necrosis of the myocardium took place, and the experiment was terminated by intrapericardial hemorrhage. The degree of reaction necessary to produce polyserositis had to be learned by experience, and unfortunately a large number of dogs were used. Under favorable circumstances polyserositis developed from one to three months after the solution was applied to the pericardium. It was our experience that when polyserositis developed, the condition progressively became more marked and death usually occurred within a few days after ascites was clinically demonstrable, unless pericardiectomy was performed. In no experiment did the dog recover spontaneously. In the first experiments we were novices in the performance of the operation for the relief of the condition and we needlessly lost a number of animals with marked polyserositis. It required considerable experience before we appreciated fully the narrow margin of tolerance for operation possessed by the dogs with polyserositis. A small anesthetizing dose of sodium iso-amyl-ethyl barbiturate or the induction of ether anesthesia was sometimes lethal. The anesthetic and the aeration of the lungs had to be observed cautiously and controlled. The operating table was heated. The operation had to be carried out with dispatch.

EXPERIMENTS

The following protocols were selected from about fifty experiments, not only to illustrate spectacular cures effected by pericardiectomy, but also to demonstrate certain important considerations in the operation, the pathology of the condition and points of clinical interest in the course of the experiment.

EXPERIMENT 1 (DOG 29-17).—The dog, a female collie, weighed 24 Kg. Oct. 23, 1929: Surgical solution of chlorinated soda was injected into the pericardium.

December 7: The pulse rate was 128, and the venous pressure 40 mm. of water. There was an audible systolic rub. The animal had shown no ascites, cyanosis or other signs of decompensation.

7. Eyster, J. A. E.: The Clinical Aspects of Venous Pressure, New York, The Macmillan Company, 1929.

December 11: The operation was repeated. The pericardium was only slightly thickened. It was everywhere adherent to the heart. The adhesions were separated and the pericardium was lavaged with surgical solution of chlorinated soda. This dog was examined at weekly intervals. Venous pressure readings were 0, 28 and 25 mm. of water. The pulse rate was never above 136 per minute. No cyanosis or other signs of decompensation appeared.

March 15, 1930: The animal was killed. At autopsy the left lung was found to be adherent to the pericardium. The pericardial cavity was completely obliterated by fibrous adhesions, but the pericardium was not thickened. There was no exudate on the liver and no congestion of the viscera.

Comment.—This experiment showed that obliteration of the pericardial cavity by adhesions need not produce cardiac disability. Unless the pericardium was thickened and contracted so as to interfere with the expansion of the heart or unless there were firm adhesions to surrounding resistant structures, decompensation did not occur.

EXPERIMENT 2 (DOG 29-6).—A female collie weighing 9.2 Kg. was used.

Aug. 20, 1929: The pericardial cavity was irrigated with surgical solution of chlorinated soda.

October 3: Fluid was present in the abdomen and chest. The subcutaneous tissues were edematous. The pulse rate was 140 per minute. The red blood cell count was 4,984,000. The minute volume output of the heart was 467 cc. This represents about one-fourth the normal cardiac output for a dog of this size. Pericardiectomy was decided on. Sodium iso-amyl-ethyl barbiturate, 0.5 Gm., was given intravenously. The abdomen was tapped and the dog died. Generalized edema of the subcutaneous tissues was present. The right side of the chest contained 210 cc., and the left side 140 cc., of clear fluid. The lungs weighed 85 Gm.; they were air containing and showed no edema. The heart seemed to be smaller than normal. The pericardium was thickened and appeared to have shrunken. It was everywhere adherent to the heart by fibrous adhesions. There were no pockets of fluid within the pericardium (fig. 1). The abdomen contained 1,320 cc. of clear fluid. The liver was slightly congested and there was a layer of fibrin between its lobes. It weighed 500 Gm. The spleen and kidneys were not congested.

Comment.—In this experiment polyserositis and edema of the subcutaneous tissues developed within six weeks after the solution was introduced into the pericardial cavity (fig. 1). The minute volume output of the heart before death was greatly decreased. The pericardium and the heart seemed to be smaller than normal. Undoubtedly pericardiectomy would have relieved the heart of this impediment, as shown by other experiments.

EXPERIMENT 3 (DOG 29-29).—A male mongrel collie weighed 15.3 Kg. Dec. 3, 1929: Surgical solution of chlorinated soda was injected into the pericardial cavity.

December 21: A roentgenogram showed that the cardiopericardial shadow had definitely increased in size. The venous pressure was 170 mm.

December 30: There were no signs of fluid in the chest or abdomen and no edema. The venous pressure was 112 mm. The dog was inactive and had lost its appetite.

Jan. 6, 1930: Edema of the scrotum had developed. Fluid was present in the abdomen. The circumference of the abdomen was 56 cm.; the dog weighed 17.2 Kg. The respiratory rate was 36 per minute, the pulse rate 180 and the venous pressure 160 mm.

January 13: In roentgenograms the cardiopericardial shadow had definitely increased in size. The diaphragm was elevated. Fluid was present in the chest. The animal weighed 17.8 Kg. The respiratory rate was 36 per minute, the pulse rate 184 and the venous pressure 220 mm. A systolic rub was heard over the left side of the chest. The dog was listless and inactive. The circumference of the abdomen was 62 cm. Electrocardiograms taken with the dog lying on the right side and then on the left side showed a shift of the electrical axis with change of

Fig. 1 (experiment 2, dog 29-6).—The heart and the pericardium seemed to be smaller than normal. The pericardium was thickened and generalized intrapericardial adhesions were seen. The Pick syndrome was present.

position. The minute volume output of the heart was 1,480 cc. (The normal minute volume output of the heart in a dog of this weight is about 2,200 cc.) In inserting the aspirating needle through the pericardium and heart for specimens of ventricular blood, definite resistance was encountered in passing the needle through the pericardium.

January 16: The weight of the dog was 18.275 Kg. The circumference of the abdomen was 68 cm. The pulse rate was 172 per minute. Respirations were labored, the rate being 44 per minute. An operation was performed. The subcutaneous tissues and muscles were edematous and the veins of the thoracic wall were congested. Several inches of the left fifth rib were removed. The chest contained 300 or 400 cc. of bloody fluid. The pericardium was exposed. The

heart was pulsating feebly. It was apparent that immediate measures were necessary to free the heart from its encumbrance. We cut through the thickened pericardium and felt with the finger for the plane of cleavage between the heart and the pericardium. Unfortunately, the plane could not be found and the finger dissected into the wall of the left ventricle. After considerable difficulty, the pericardium was dissected free, but at this time the heart was no longer pulsating. Epinephrine was injected into the heart, which was then massaged. A few feeble pulsations were obtained, but they did not become forceful.

Fig. 2 (experiment 3, dog 29-29).—Several layers of laminated scar involved both the parietal pericardium and the epicardium. It was impossible, even in the specimen at necropsy, to remove this scar completely without injury to the coronary vessels and the myocardium. The tear in the muscle was made at operation in the attempt to find a line of cleavage.

The specimen was of great interest (fig. 2). The adherent pericardium and epicardium appeared similar to those in the human being in certain conditions. These structures were several millimeters in thickness and were definitely laminated. After we had removed from the heart what we considered to be the parietal pericardium there remained another fibrous layer over the surface of the heart; after the latter layer was dissected free there was in places still another

layer intimately involving the coronary vessels and myocardium. It was impossible to remove the entire scar with the scalpel without cutting down to the muscle fibers and the coronary vessels. If attempts at a dissection of this kind were carried out on the pulsating heart, the possibility of cutting coronary vessels would be great. The heart weighed 160 Gm.

Microscopically, the thickened pericardium and epicardium were composed of connective tissue elements compactly arranged. It was everywhere hyalinized and

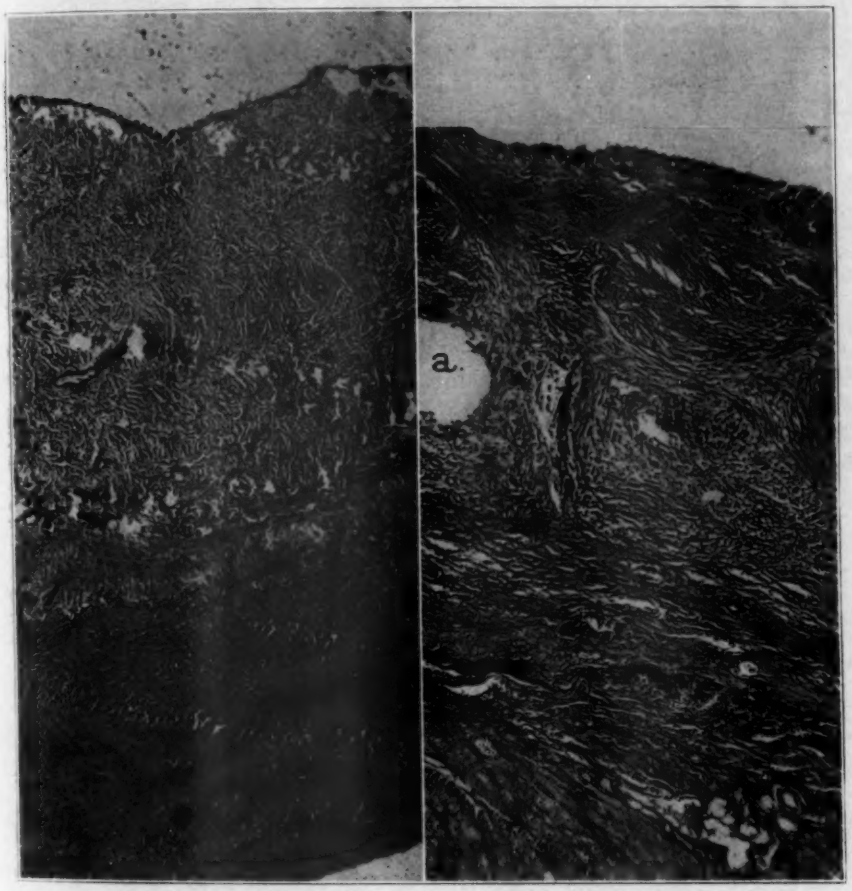

Fig. 3 (experiment 3, dog 29-29).—Deposition of scar involving parietal pericardium and epicardium. *A* was separated from *B* at operation. Another plane of cleavage is present in *B* at *a*. The scar did not deeply invade the myocardium appearing at the bottom in *B*, but the coronary vessels were involved in the scar.

contained few blood vessels. There was little, if any, leukocytic infiltration. This hyalinized tissue was intimately adherent to the parietal pericardium and epicardium (fig. 3). The scar tissue formation was limited by the epicardium and it did not invade the underlying myocardium.

The lungs were air containing, weighed 130 Gm. and showed no edema or consolidation.

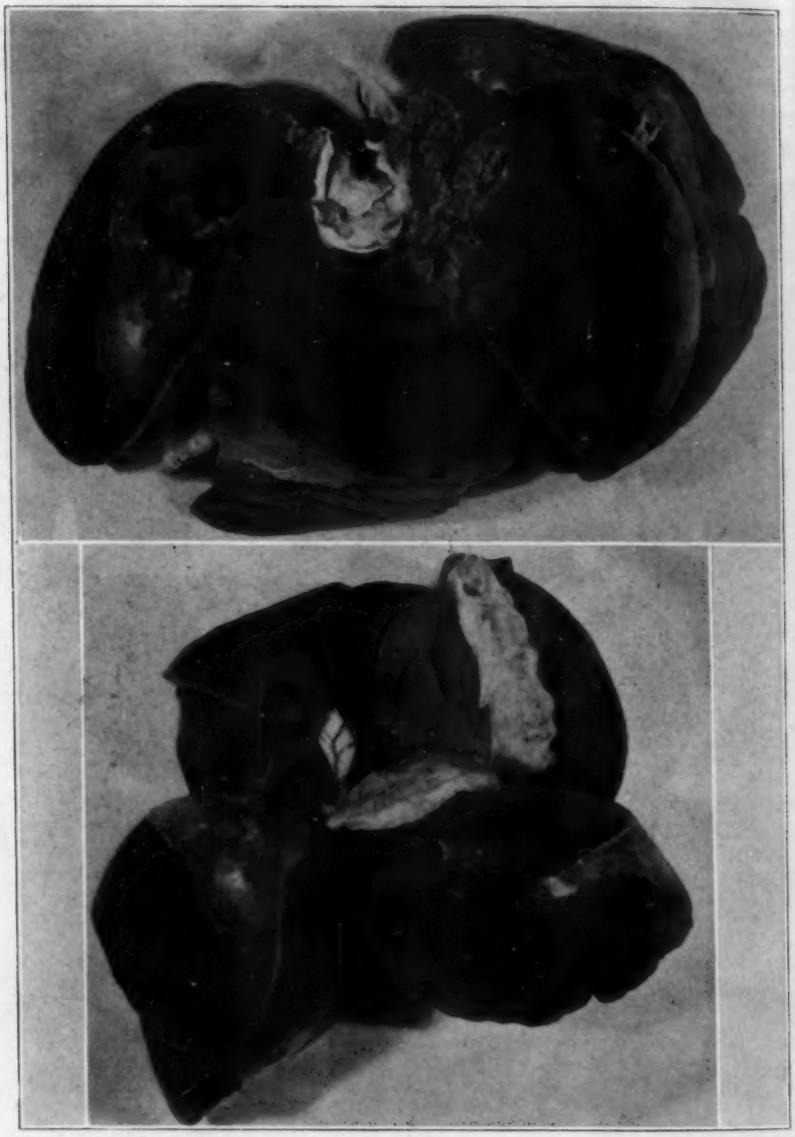

Fig. 4 (experiment 3, dog 29-29).—On the surface of the liver a thin fibrinous exudate was present; between the contiguous lobes there was a thick deposition of fibrin. These fibrin deposits developed in the course of six weeks. It is probable that had the experiment continued over a sufficiently long period of time the classic "zuckergussleber" might have formed.

The abdomen contained 2,000 cc. of straw-colored fluid. The liver was markedly congested and weighed 560 Gm. A point of great interest was the presence of a thin layer of fibrin on the diaphragmatic surface of the liver (fig. 4). This fibrinous layer lay in thick plaques between the various lobes of the liver, from which it was easily separated. The fibrin was arranged in laminae and was avascular. Where it was attached to the liver there was considerable infiltration with round cells, but elsewhere it contained only an occasional leukocyte (fig. 5).

Fig. 5 (experiment 3, dog 29-29).—A laminated exudate of fibrin, devoid of leukocytes and loosely attached to the capsule, was present on the liver.

The capillaries around the central veins of the liver were distended with blood, and the parenchyma in these areas contained an increased amount of fat.

The spleen weighed 42 Gm. and revealed some congestion. The kidneys weighed 83 Gm. and showed capillary engorgement.

Comment.—Although the pericardium and the epicardium were everywhere scarred and adherent, the electrical axis of the heart shifted with change in position. In this case we failed to relieve the adhesive peri-

carditis by operation chiefly because we delayed operation to the point where death from decompensation was imminent. The dog was waterlogged, and there was no cardiac reserve to make the operation successful. Complete resection of the scarred pericardium by sharp dissection was impossible even at necropsy. The involvement of epicardium and coronary vessels with scar was so intimate that the danger of injuring coronary vessels in the dissection was great (figs. 2 and 3). This possible danger undoubtedly may exist in certain cases in the human being and may add to the hazard of the operation.

The thickened, leathery pericardium gave a definite sense of resistance to the aspirating needle when the ventricles were tapped for specimens of blood. This sense of resistance could perhaps be utilized clinically in the human being as a diagnostic adjunct in questionable cases of adhesive pericarditis.

EXPERIMENT 4 (DOG 29-35).—A male mongrel weighed 9.8 Kg. Dec. 11, 1929: The pericardial cavity was irrigated with surgical solution of chlorinated soda. A preoperative roentgenogram showed the transverse diameter of the heart to be 6.5 cm. and the longitudinal diameter 9.8 cm.

December 24: The general condition was good and there was no evidence of circulatory failure. The minute volume output of the heart was 741 cc. The venous pressure was 90 mm. There were no signs of fluid. The pulse rate was 140 per minute.

Jan. 6, 1930: There seemed to be no change; the weight was 8.8 Kg.

January 13: The weight was 10.7 Kg. The venous pressure was 210 mm. and the pulse rate 156 per minute. There was slight edema of the scrotum and apparently some fluid in the chest and abdomen. Electrocardiograms showed no shift of the electrical axis of the heart with change of position. The circumference of the abdomen was 52 cm. The transverse diameter of the heart was 6 cm. and the longitudinal diameter 8.4 cm., as shown by the roentgenogram.

January 16: There was marked ascites and evidence of fluid in the chest. The pulse rate per minute was 158 and the respiratory rate 24. The circumference of the abdomen was 56 cm. The scrotum was edematous. It was decided to make another cardiac output determination before pericardiectomy was carried out. During the cardiac puncture the dog coughed up a little blood and died. At autopsy the chest was filled with bloody fluid and there was a large amount of pink fluid in the abdomen. The soft tissues were edematous and the veins were distended. Both lungs were extensively adherent to the pericardium, and there were adhesions to the scar of the thoracic wall on the left side. The pericardio-diaphragmatic ligaments were thickened and tense. The parietal pericardium was everywhere tightly adherent to the heart and in some places could be separated only by sharp dissection (fig. 6). Over the right ventricle the myocardium was dark, as though it had been burned deeply with surgical solution of chlorinated soda. The lungs were edematous, and the liver was congested. There was a thin fibrinous exudate over the surface of the liver.

Comment.—In the light of later experience it would seem that pericardiectomy should have been carried out earlier. The diminution in

the size of the heart in this dog by reason of shrinkage of the pericardium was marked. The fixation of the electrical axis of the heart was explained by the adhesion to the wall of the chest and by the thick tense pericardio-diphragmatic ligaments, which acted as guy wires, holding the heart firmly in position (fig. 6).

EXPERIMENT 5 (DOG 29-5).—A male mongrel police dog weighed 22.2 Kg. Aug. 19, 1929: Surgical solution of chlorinated soda was injected into the pericardial cavity.

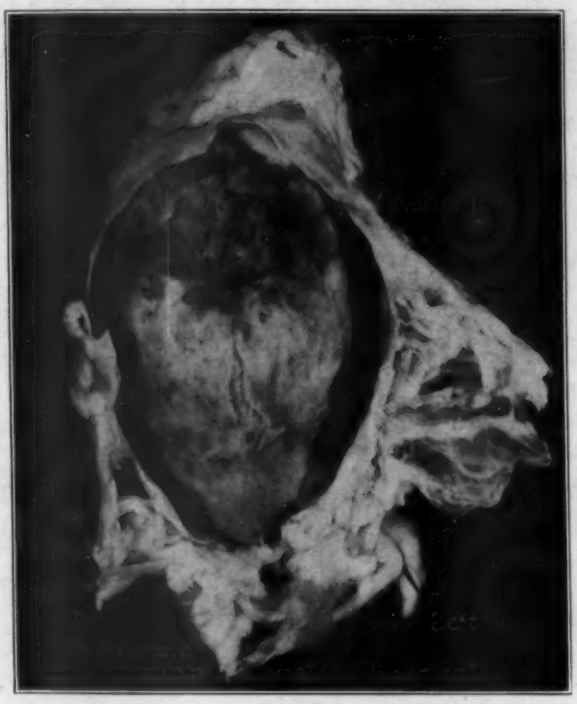

Fig. 6 (experiment 4, dog 29-35).—The pericardium is opened and dissected from the epicardium. The adhesion to the chest wall and the thickened pericardio-diaphragmatic ligaments account for the fixation of the electrical axis of the heart with change of position.

October 1: A systolic friction rub was heard over the right side of the chest. The jugular veins were distended. The tongue seemed to be slightly cyanotic. There was no demonstrable ascites or fluid in the chest. The dog weighed 18.4 Kg.

October 12: The abdomen was greatly distended with fluid, and edema of the scrotum and of the paws was present. The cardiac sounds were faint. The rub had disappeared. The tongue was cyanotic and the jugular veins were distended. The chest contained fluid. The pulse rate was 156 per minute and the respiratory rate 20. The temperature was normal; the red blood cell count was 4,480,000

and the hemoglobin content 60 per cent. The minute volume output of the heart was 1,684 cc. (the normal minute volume output for a dog of this size is well over 3,000 cc.); 2,260 cc. of straw-colored fluid was removed from the abdomen. The roentgenograms showed a large globular heart.

October 15: Marked edema and polyserositis were present. The minute volume output of the heart was 908 cc. Aspiration of the abdominal cavity yielded 540 cc. and that of the pericardial cavity 14 cc.

Pericardiectomy was decided on, but the injection of 0.5 Gm. of sodium isoamyl-ethyl barbiturate was followed by the death of the dog. The right side of the chest contained 400 cc., and the left side of the chest 50 cc., of bloody fluid. There was 300 cc. of clear fluid in the abdomen. The pericardium was thickened. There were no extrapericardial adhesions. The pericardial cavity contained about 100 cc. of clotted blood. There were some fibrinous adhesions between the pericardium and the heart. The lungs were everywhere air containing and showed no edema; they weighed 262 Gm. The surface of the liver was adherent to the peritoneum by fibrinous adhesions, and between contiguous lobes of the liver a well marked fibrinous exudate was present. The liver, spleen and kidneys showed capillary congestion.

Comment.—The acutely developing cardiac failure in the foregoing experiment was caused partly by the tamponade produced by the blood clot in the pericardial cavity. A marked degree of cardiac decompensation developed. Fluid was present in the chest and in the abdomen. Subcutaneous edema had developed. The minute volume output of the heart was greatly reduced. The cardiac reserve was nil at the time we intended to perform pericardiectomy. This operation should have been performed before the decompensation became marked.

EXPERIMENT 6 (DOG 29-21).—A male mongrel collie weighed 10.1 Kg. Nov. 14, 1929: Surgical solution of chlorinated soda was injected into the pericardial cavity.

December 7: The weight of the dog was 12.9 Kg. There was no demonstrable fluid in the chest and no edema of the extremities. The jugular veins were dilated and the venous pressure was 55 mm. Five hundred cubic centimeters of pink fluid was removed from the abdomen.

December 9: The dog was somewhat listless and weak. The minute volume output of the heart was 1,316 cc. (The normal minute volume output for a dog of this weight is about 1,800 cc.)

December 10: Fluid had formed in the abdomen, and it was apparent that an immediate operation was necessary to save the dog. Edema was present in the tissues of the chest and abdomen. The minute volume output of the heart was 1,451 cc. In drawing the samples of blood from the heart it was noticed that a definite resistance was met by the aspirating needle in passing through the pericardium. The abdomen was tapped, and 500 cc. of straw-colored fluid was obtained. The dog was placed on a warm operating table, and ether anesthesia was started. The left fifth rib was removed. There was no free fluid in the chest. The lung was found to be adherent in small areas to the pericardium. The pericardium was picked up and incised. It was about 3 mm. thick, tough and fibrous. Much to our surprise, the pericardium was not adherent anywhere to the heart. The left phrenic nerve was dissected from the pericardium. The pericardium was then widely resected over each side of the heart, well up over

the auricles. At this point the tube slipped out of the trachea and the anesthetist inserted it into the esophagus. By the time the tube was reinserted into the trachea the heart was at a standstill. After the administration of epinephrine the heart began to pulsate, but the pulsations did not become forceful. Closure was carried out, but by the time the wound was sutured the heart had stopped beating.

The epicardium was covered by a thin film of fibrous tissue, which subsequently might have impaired the diastolic expansion or filling of the heart (fig. 7). The heart seemed to be smaller than normal; it weighed 76 Gm. Microscopically, the scar lay entirely exterior to the epicardium, showing no involvement of the underlying elements. The scar of the parietal pericardium was several millimeters thick and showed some infiltration with leukocytes. The lungs weighed 103 Gm. and were moderately edematous. Microscopically, a few scattered areas of lobular pneumonia were found, together with well marked congestion. The abdomen contained 200 cc. of fluid. The liver was congested and weighed 530 Gm. A fibrinous exudate was present between contiguous lobes of the liver. Microscopically, the surface of the liver showed a fibrinous exudate infiltrated with leukocytes. There was some congestion around the central veins. The kidneys showed some capillary congestion, especially in the glomerular tufts.

Comment.—This experiment was especially instructive in that the fully developed syndrome of Pick's disease was produced without any adhesions between the pericardium and epicardium. In this case the impediment to the circulation was produced by scar tissue formation in the parietal pericardium, without any adhesions to the heart. Pericardiectomy should have been followed by a beneficial result. Had the epicardial scar (fig. 7) continued to increase, however, polyserositis might have developed again.

EXPERIMENT 7 (DOG 29-36).—A female mongrel shepherd dog weighed 18.6 Kg. Dec. 11, 1929: The pericardial cavity was irrigated with surgical solution of chlorinated soda.

December 18: The minute volume output of the heart was 2,366 cc.

December 21: The venous pressure was 110 mm. and the weight of the dog 20.8 Kg. Respirations were labored, the pulse was rapid, and there was some dulness over the right side of the chest. A roentgenogram showed haziness and increased density (fluid).

December 23: Respirations were labored, and the dog appeared sick. The minute volume output of the heart was 2,524 cc. There was clinical evidence of fluid in the chest. No abdominal fluid could be demonstrated. There was superficial infection of the previous incision. Ether anesthesia was administered and the left fifth rib resected. There was about 500 cc. of serosanguineous fluid in the chest. The pericardium was tense, leathery and discolored by hemorrhage. It was incised from the apex to the base. There was no free pericardial fluid, though in some places organizing clots were found. The adhesions, which were present everywhere over the heart, were easily separated. The left phrenic nerve was dissected free and the pericardium excised on both sides as far as possible. The heart seemed to dilate as the restricting pericardium was removed, and the color of the tissue improved. The fluid was removed from the chest, and the wound was closed in layers with silk. On the following day the animal seemed to be in better condition, more active and bright. The pulse rate per minute was 164.

December 26: The pulse rate per minute was 156 and the respiratory rate 36; respirations were somewhat labored but better than before operation. The venous pressure was 68 mm. of water. The dog was stronger, not so listless and eating well. Later in the day, it was noticed that the wound had broken open into the pleura, probably as a result of the infection in the wall of the chest from the previous operation. It was closed at once, but showed little tendency to heal.

Jan. 4, 1930: Death occurred from infection. Necropsy showed empyema and epicardial infection. The remaining fringes of pericardium were adherent to the heart. The abdomen contained no fluid and there was no exudate between the lobes of the liver.

Comment.—Failure in this case was due to the occurrence of infection. The early postoperative course, with marked improvement in the

Fig. 7 (experiment 6, dog 29-21).—The pericardium was resected at operation. It was thickened but nowhere was it adherent to the heart. The heart seemed to have been compressed by the shrinking of the parietal pericardium. Resection of the pericardium undoubtedly would have been followed by improvement in the circulation. The epicardium was glazed with a film of scar tissue which subsequently might have thickened sufficiently to impair the filling of the heart.

general condition and a marked fall in the venous pressure, indicated that the operation was effective, and that the circulation would have improved if the infection had not occurred.

Experiment 8 (Dog 29-31).—A male collie weighed 19.5 Kg. Dec. 5, 1929: Surgical solution of chlorinated soda was injected into the pericardial cavity.

December 21: The cardiopericardial roentgenogram was larger than normal, measuring 9.4 cm. in the transverse diameter. The venous pressure was 130 mm.

December 24: The dog was so weak that it could not stand. Respirations were labored. Cyanosis of the tongue was present. The pulse was rapid and weak. Eight hundred cubic centimeters of pink fluid was tapped from the abdomen and 200 cc. of bloody fluid from the chest.

December 26: The soft tissues over the abdomen and chest were markedly edematous. Dyspnea and cyanosis were marked. The pulse was scarcely perceptible, its rate being about 200 per minute. The dog was placed on a warm operating table and anesthetized with ether. The left fifth rib was removed and the chest was opened. Four hundred cubic centimeters of bloody fluid was removed from the chest. The heart was at a standstill. Epinephrine was injected into it, and it began to pulsate feebly. The pericardium and its contents appeared dark, resembling liver. The lung was adherent to the pericardium and was congested. An incision was quickly made into the pericardium, which was several millimeters thick, tense and adherent to the heart. A line of cleavage was found, and with the finger the pericardium was freed from the heart. Several pockets of bloody fluid were evacuated during this procedure. The heart seemed to dilate slightly after it was dissected free from the pericardium, but its pulsations were feeble. We quickly excised the pericardium, and in our haste we sacrificed the left phrenic nerve (fig. 8). The tongue of lung that was adherent to the pericardium was ligated and excised. As closure was carried out, the color of the tissues seemed to improve. We feared that the operation would not save the dog.

December 31: The shadow of the heart, as shown by a roentgenogram, measured 8.4 cm. in the transverse diameter. This represented a decrease of 1 cm. from the measurement made before operation; this difference undoubtedly could be accounted for by the presence of small pockets containing clotted blood between the heart and the pericardium.

Jan. 3, 1930: Edema of the tissues persisted. The pulse rate was 164 per minute and the respiratory rate 30. The venous pressure was 105 mm. The circumference of the abdomen was 61 cm. The dog was able to walk and showed improvement as compared with its condition immediately before operation.

January 6: The dog had undergone striking improvement. The subcutaneous edema had completely disappeared. The ascites was much less; the circumference of the abdomen was 56 cm. Respirations were not labored, the rate being 24 per minute; the pulse rate was 140, the venous pressure 80 mm. and the weight of the animal 19 Kg.

January 13: The dog was very active; the pulse rate was 160, but this rapid rate was caused by excitement. The appetite was good. The venous pressure was 70 mm.

January 20: The dog was active; the venous pressure was 65 mm., the pulse rate 144 per minute and the respiratory rate 18. The weight of the dog was 19.2 Kg. and the circumference of the abdomen 62 cm. Fluid was forming in the abdomen. Slight edema of the scrotum was present.

January 27: The venous pressure was 170 mm.

February 10: The weight was 21 Kg. The circumference of the abdomen was 71 cm. The pulse rate was 156 per minute. The abdomen was distended with fluid. The venous pressure was 240 mm. Eighteen hundred cubic centimeters of fluid was tapped from the abdomen. The shadow of the heart in roentgenograms measured 7.7 cm. in the transverse diameter. A shadow was present over the right margin of the heart. We concluded that the portion of the pericardium over the venae cavae that could not be resected at the previous operation was producing the circulatory failure that had been developing since January 20. The exposure through the left side of the chest was inadequate for the complete resection of

the pericardium in the region of the venae cavae. We interpreted the decrease in the size of the cardiac shadow in the roentgenogram as being due to the formation and contracture of epicardial scar. The electrocardiograms showed no shift in the electrical axis of the heart with change of position. The dog was placed on a warm operating table, and ether was administered. The right fifth rib was

Fig. 8 (experiment 8, dog 25-31).—*A*, segments of parietal pericardium excised from the left side of the heart at the first operation. *B*, segments of parietal pericardium excised from the right auricle and ventricle at the second operation. The importance of complete excision of the scar was emphasized.

resected and the chest was opened. There was no fluid. Mediastinal fat was adherent to the heart on the right side. This was sufficient to prevent shifting of the heart with change of position. A segment of pericardium was found adherent to the right auricle and the venae cavae, also extending over a small area of the

right ventricle. The parietal pericardium was dissected from these structures by the finger. As the inferior vena cava was approached, a broad band of thickened scar was found extending from the parietal pericardium between the vena cava and the auricle. This scar produced partial obstruction to the vena cava (fig. 9). The band was incised and its pedicle ligated. When it was released, it disappeared from view. A segment of pericardium equivalent to 30 sq. cm. was resected (fig. 8). The epicardium was covered with fibrous tissue. The right phrenic nerve was involved in the pericardial scar, and it was accidentally sacrificed. At the completion of the operation the respiratory movements were costal, each phrenic nerve having been sacrificed.

February 20: The paralysis of the diaphragm greatly interfered with respiration. The dog had undergone a remarkable improvement since the last operation,

Fig. 9 (experiment 8, dog 29-31).—Appearance of the scar that impaired the filling of the right side of the heart and partially obstructed the inferior vena cava. The failure to resect this scar at the first operation and the subsequent contracture of it brought about the recurrence of the Pick syndrome.

but circulatory embarrassment persisted. The pulse rate was 120 per minute. The venous pressure was 125 mm. Seven hundred cubic centimeters of fluid was tapped from the abdomen. The cardiac shadow in the roentgenogram measured 7.5 cm. in the transverse diameter. The heart had undergone a progressive decrease in size since December 26, when pericardiectomy was performed. This was interpreted as due to the formation and contraction of epicardial scar. On each side the diaphragm was elevated and encroached on the pleural space.

March 6: The venous pressure was 130 mm.

March 7: Death occurred. The subcutaneous tissues showed slight edema. The chest contained 2,000 cc. of fluid that looked like a mixture of chocolate and

milk. This fluid had a specific gravity of 1.014, contained much fat and many lymphocytes and was not infected. It resembled lymph from the gastro-intestinal tract. The heart was free in the mid-chest and was not adherent to any of the surrounding structures. The heart was "iced" with a film of epicardial scar (fig. 10), which undoubtedly had impaired its function. Microscopically, the scar tissue consisted of fairly dense connective tissue elements containing areas that stained blue with hematoxylin and resembled tissue containing calcium. There was no infiltration or fibrosis of the adjacent muscle fibers, but here and there was a deposition of fat. The parietal pericardium removed at operation was less densely organized. It contained many blood vessels and deposits of fibrin. The lungs were edematous and microscopically showed considerable fibrosis. The

Fig. 10 (experiment 8, dog 29-31).—The parietal pericardium had been removed at operation. This specimen shows the heart with its encasement of epicardial scar. Although this epicardial scar was adherent to the myocardium, it was possible to dissect it with the scalpel without injury to the myocardium and coronary vessels.

abdomen contained 2,500 cc. of pink fluid with a specific gravity of 1.020. The liver weighed 950 Gm.; it was markedly congested. The contiguous surfaces of the various lobes of the liver showed an exudate of fibrin, in places 2 mm. thick. Each kidney weighed 80 Gm. and showed marked venous and capillary congestion.

Comment.—The foregoing experiment brought out several important considerations. A marked degree of polyserositis and subcutaneous edema developed, and it was feared that the cardiac reserve was too

small to tolerate pericardiectomy. The pericardium was separated and excised while the heart was at a standstill. The exposure through the left side of the chest was inadequate to permit complete resection of the pericardium. The region where the venae cavae entered the right auricle was inaccessible through this exposure. A striking improvement followed the operation. During the succeeding three weeks, however, decompensation developed. An operation was again carried out. An exposure was made through the right side of the chest. A segment of thickened pericardium was found adherent to the heart where the venae cavae entered the right auricle, and a band of thickened pericardium caused a partial obstruction to the inferior vena cava (fig. 9). The fact that no shift of the electrical axis occurred with change of position was readily accounted for by the adhesions between the right auricle and adjacent structures. This portion of the pericardium was excised (fig. 8) and the circulation again improved. During the following month the size of the heart, as shown by roentgenograms, progressively decreased and decompensation again developed. A thick layer of fibrous tissue had formed over the epicardium; this epicardial scar embarrassed the circulation as did the parietal pericardium which had been excised at the preceding operations (fig. 10).

The advantage of a bilateral exposure of the pericardium at operation was emphasized in this experiment. The subject will be discussed more fully.

The probable explanation of the decompensation is as follows: During the first period of decompensation, fluid was present in the chest and the lungs were congested. This may have indicated an impairment in the filling of the left side of the heart. The ascites and subcutaneous edema that were also present may have indicated an impairment in the filling of the right side of the heart. The first pericardiectomy relieved the left side of the heart, and pulmonary edema and hydrothorax were absent during the second period of decompensation. The impairment to the filling of the right side of the heart was relieved temporarily by the second pericardiectomy. Then contraction of epicardial scar occurred. The heart decreased in size. The filling of the heart again became impaired, and there was evidence of both right-sided and left-sided failure. This is an excellent example of the effects on the dynamics of the circulation brought about (1) by a generalized restriction to cardiac function, (2) by restoration of the left side and restriction of the right side, (3) by restoration of the right side and (4) by subsequent bilateral restriction of the heart and failure of both ventricles.

The development of epicardial fibrosis which produced the third instance of decompensation in this experiment has certain clinical

interest. One of the deep-seated objections held by physicians to this operation is that even though the pericardial scar can be excised, scar tissue will form again on the epicardium. The objection was valid in this experiment. The heart, however, did not become adherent to any of the surrounding structures even though an active process of fibrosis was taking place on its surface. It was noteworthy, however, that this epicardial scar could be dissected from the myocardium; while it may have been a difficult and hazardous dissection on a pulsating heart, we had the impression that it could have been done successfully (fig. 10).

Experiment 9 (Dog 29-25).—A female collie weighed 17 Kg. Dec. 2, 1929: Surgical solution of chlorinated soda was injected into the pericardial cavity.

December 24: The minute volume output of the heart was 1,517 cc.

December 28: The minute volume output of the heart was 1,326 cc.

December 30: The abdomen seemed to be enlarged. The venous pressure was 80 mm. There were no signs of fluid in the thorax and no edema of the subcutaneous tissues. The pulse rate was 120 per minute. The electrocardiogram showed a questionable shift of the electrical axis with change of position.

Jan. 6, 1930: The abdomen was enlarged. The mammary glands were hypertrophied, but did not contain milk. It was thought that the enlargement of the abdomen was due to pregnancy. A few cubic centimeters of fluid was tapped from the abdomen. The venous pressure was 75 mm. The pulse rate was 140 per minute.

January 9: The dog was listless. The pulse rate was 152 per minute and the respiratory rate 36. The venous pressure was 375 mm. The minute volume output of the heart was 1,339 cc. A definite resistance to the passage of the aspirating needle through the pericardium was encountered. Again only a few cubic centimeters of fluid could be aspirated from the abdomen, and the increase in the size of the abdomen was believed to be due to pregnancy. The cardiopericardial roentgenograms showed a decrease in size and definitely globular shape (fig. 11). This globular contour was interpreted as due to shrinkage of the pericardium. The compression thus produced on the heart caused it to assume a more globular shape.

January 10: The dog was placed on a warm table and ether anesthesia was given. The left fifth rib was removed and the chest was opened. There was no fluid. A few adhesions were found between the left lung and the pericardium. The pericardium was globular and tense, as though distended by its contents. An incision was made in it; in doing this a small coronary vein was cut. The pericardium was several millimeters thick. Adhesions everywhere tightly bound the pericardium to the heart. These were separated by blunt dissection. The left auricular ear was adherent to the ventricle. The left phrenic nerve was dissected from the pericardium as was also the adherent lung. The parietal pericardium was then almost completely excised. The epicardium did not seem to be scarred. The heart throughout tolerated the procedure well. There was no bleeding from its surface. The wound was sutured.

January 27: The dog was active and in good condition. It had had puppies a week before. The pulse rate was 128 per minute and the respiratory rate 16. The venous pressure was 55 mm.

February 10: The venous pressure was 50 mm. A roentgenogram showed that the heart had returned to normal in size and shape. It was now elongated and somewhat larger than before the pericardium was resected (fig. 11).

March 3: The minute volume output of the heart was 1,759 cc. The weight of the dog was 12.8 Kg. The sense of resistance previously obtained as the aspirating needle penetrated the parietal pericardium was not noted. The pulse rate was 108. There was no edema.

April 2: The animal weighed 14.2 Kg.; it was in good condition and active, with a good appetite. The venous pressure varied from 10 to 20 mm. There was no evidence of circulatory abnormality.

May 1: The dog was in excellent condition. The venous pressure was 20 mm. The size and shape of the heart appeared the same as in the previous roentgenogram.

Microscopically, the parietal pericardium consisted of hyalinized connective tissue containing few cells and measuring about 2 mm. in thickness. The surface of this scar in contact with the heart possessed a layer of loose areolar tissue which may have allowed slight movement between the heart and the scar.

Fig. 11 (experiment 9, dog 29-25).—Roentgenograms showing the change in contour of the heart brought about by shrinkage and thickening of the pericardium. *A* represents the condition after pericarditis was produced. The heart is globular and somewhat smaller than normal. *B* represents the condition after pericardiectomy. The heart is elongated and has assumed its normal size and contour.

Comment.—In this experiment the injection of surgical solution of chlorinated soda into the pericardial cavity was followed by generalized adhesive pericarditis. The condition had not progressed sufficiently long to produce polyserositis. The roentgenograms showed that the cardiopericardial shadow had decreased in size and had assumed a globular shape (fig. 11). This undoubtedly was caused by shrinkage of the pericardium and compression of the heart. Because of this compression the filling of the heart was impaired, the venous pressure increased and the cardiac output decreased. Pericardiectomy restored the dog to good health. The heart assumed its normal size and shape.

The venous pressure fell to normal. The improvement following the operation was progressive and there was no evidence of epicardial scar formation. The heart was not displaced by adhesions. The electrocardiogram showed a shift in the electrical axis with change in position. There was no evidence of myocardial involvement.

EXPERIMENT 10 (DOG 29-43).—A female mongrel bulldog weighed 16.7 Kg. Jan. 17, 1930: The pericardial cavity was irrigated with surgical solution of chlorinated soda.

January 27: The dog was active and seemed to be in good condition. It weighed 14.8 Kg. There was no evidence of decompensation. The circumference of the abdomen was 42 cm. The pulse rate was 180 per minute and the venous pressure 67 mm.

February 10: Polyserositis was developing. The circumference of the abdomen was 51 cm. The animal weighed 16 Kg. The pulse rate was 164 per minute and the respiratory rate 16.

February 21: The venous pressure was 260 mm. The circumference of the abdomen was 63 cm.; 900 cc. of straw-colored fluid was tapped from the abdomen and the weight after tapping was 17.7 Kg. Fluid was present in the chest. The cardiopericardial shadow, as seen in roentgenograms, had increased in size.

February 22: The dog was very weak. The tongue was cyanotic. Edema developed in the subcutaneous tissues, especially in the neck. We feared that the dog could not live another day, and an operation was immediately carried out. The animal was placed on a warm operating table and anesthetized with ether. As the incision was made in the thoracic wall, we noticed that there was no bleeding. Pulsation of the heart could not be felt. The chest was quickly opened and the free fluid mopped out. The heart was at a standstill. Epinephrine did not revive the heart, and the situation looked hopeless. The pericardium was tense and thickened. An incision was made into it, and the myocardium to which the pericardium was adherent was also cut. The wound in the heart bled profusely. The plane of cleavage between the thickened pericardium and the heart was found by the finger. In places sharp dissection was necessary to cut these adhesions. Several walled-off pockets of bloody fluid were encountered and opened. They contained approximately 75 cc. of fluid. After the adhesions were separated, the heart began to pulsate feebly. The wound in the heart was then sutured, and epinephrine was injected into the myocardium. The pulsations became stronger, and after a while were forceful. The left phrenic nerve was dissected from the pericardium. The pericardio-diaphragmatic ligaments were incised; the mediastinum was dissected from the pericardium and a wide excision of the pericardium was carried out on each side of the heart. Exposure of the region where the venae cavae entered the right auricle was difficult. The pericardium measured about 3 mm. in thickness. The fluid was removed from the chest, and closure was carried out. The dog underwent a most spectacular improvement.

March 6: The dog was active. The edema of the subcutaneous tissue seemed to have disappeared. There may have been a little fluid in the abdomen. The cardiopericardial shadow in the roentgenograms was of normal size. The venous pressure was 60 mm. The pulse rate was 136 per minute. The weight was 14.2 Kg.; the dog had lost several kilograms by diuresis.

March 19: The dog was in excellent condition. The venous pressure was 25 mm. The weight of the animal was 13.6 Kg. There was no evidence of fluid in the chest or the abdomen.

May 1: The venous pressure was 20 mm. The dog was in good condition and apparently normal in all respects.

Comment.—In this experiment the introduction of surgical solution of chlorinated soda into the pericardial cavity was followed by a profound degree of circulatory decompensation. The heart was at a standstill when pericardiectomy was carried out. The parietal pericardium was separated from the heart and several walled-off pockets containing blood-stained fluid were evacuated. The heart then began to pulsate, at first feebly; then it made a heroic response. Resection of the pericardium was carried out.

Following this operation a spectacular improvement took place. The dog became active. All signs of circulatory failure disappeared. The venous pressure decreased to normal. The edema and the fluid in the chest and the abdomen disappeared and did not reform. As far as could be determined, the dog was restored to normal health. When it was last observed, there were no signs of epicardial scar formation, fixation of the heart or myocardial weakness.

EXPERIMENT 11 (DOG 29-34).—A male bulldog weighed 16.3 Kg. Dec. 6, 1929: The venous pressure was normal (0). The cardiopericardial shadow seen in roentgenograms measured 8 cm. in its greatest transverse diameter. Surgical solution of chlorinated soda was injected into the pericardial cavity.

December 21: The cardiopericardial shadow measured 8.7 cm. in its greatest transverse diameter. The venous pressure was 105 mm. There were no signs of decompensation.

December 26: The minute volume output of the heart was 1,704 cc.

December 28: The minute volume output of the heart was 1,693 cc. The dog cooperated perfectly for determinations of cardiac output. Definite resistance was encountered by the needle in penetrating the pericardium.

December 30: The venous pressure was 50 mm. There was no evidence of decompensation.

Jan. 6, 1930: The venous pressure was 85 mm. The pulse rate was 128 per minute and the respiratory rate 18. The animal weighed 16.6 Kg. The abdomen seemed to be a little distended; the circumference was 53 cm.

January 10: The dog was listless and weak (fig. 12). Fluid was present in the abdomen; the circumference was 64 cm. The liver was enlarged. Fluid was present in the chest. Edema of the scrotum was present. The venous pressure was 190 mm. The pulse rate was 168 per minute and the respiratory rate 21. The electrocardiogram showed a shift of the electrical axis with change of position. The minute volume output of the heart was 1,107 cc. A definite resistance to the passage of the aspirating needle through the pericardium was encountered.

January 11: The cardiopericardial shadow in roentgenograms measured 8.5 cm. in its greatest transverse diameter. The abdomen was tapped and 600 cc. of straw-colored fluid was removed. The dog was placed on a warm operating table and ether was given. The left fifth rib was resected. The chest contained about 400 cc. of blood-tinged fluid. The lung was not adherent to the pericardium or to the scar in the chest. The left phrenic nerve was dissected from the surface

of the pericardium. The pericardium, which appeared dark, was picked up in forceps and incised. It was several millimeters thick and was tightly adherent to the heart. There were no pockets of fluid. A line of cleavage was found and the parietal pericardium was everywhere separated by the finger. The heart seemed to dilate and to fill better as soon as this was done. Incision of the pericardio-diaphragmatic ligaments freed the pericardium. The left pulmonary veins, the inferior vena cava, the ventricles and the base of the heart were freed from the pericardium. The excision of the parietal pericardium was almost complete. A fibrinous plaque, about 5 cm. in diameter and 4 mm. thick, lay over the

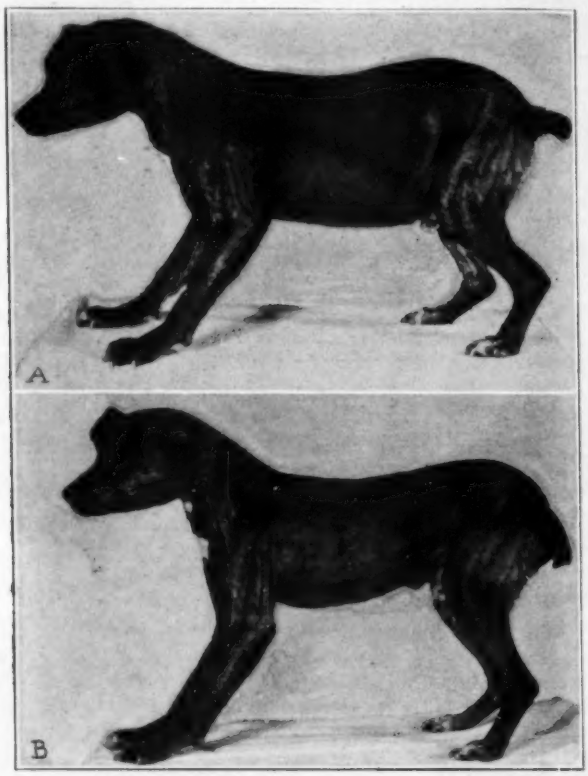

Fig. 12 (experiment 11).—*A* was taken before pericardiectomy was performed. The abdomen was distended with fluid and the dog was weak. *B* was taken five days after pericardiectomy and a paracentesis yielding 600 cc.

right auricular appendage. The surface of heart now appeared roughened and dark. There seemed to be no scar tissue left on the heart. After the heart was liberated from the pericardium it beat forcibly. We were then able to proceed slowly and carefully with the operation. After the operation the dog weighed 16.7 Kg. It was wrapped in warm blankets. Microscopically, the tissue removed consisted of connective tissue elements in various stages of organization. In places these were compact and took a deep blue stain with hematoxylin. In other places the organization was less compact, showing a lacework of fibroblasts, fibrin and red blood cells.

January 16: The dog seemed to have undergone remarkable improvement (fig. 12). Diuresis followed the operation. The polyserositis and edema seemed to have disappeared completely. The animal weighed 13.05 Kg.

January 20: The circumference of the abdomen was 46 cm. and the weight of the dog 13.1 Kg. The pulse rate was 110 per minute and the respiratory rate 16. The venous pressure was 25 mm. The dog was active and had a good appetite. The minute volume output of the heart was 2,502 cc.

January 27: The dog weighed 13.4 Kg. and was in excellent condition. The pulse rate was 100 per minute. The electrocardiogram showed a slight shift of the electrical axis with change in position. There was less slurring and notching of the Q R S complex, and R showed an increased voltage. These changes indicated an improvement of the myocardial function.

March 6: The venous pressure was 30 mm., the pulse rate 104 per minute and the weight of the animal 13.3 Kg. There were no cardiac murmurs. The minute volume output of the heart was 3,528 cc. The resistance to the passage of the aspirating needle previously noted was not observed.

Fig. 13 (experiment 11).—Three months later, the dog appeared normal.

March 19: The venous pressure was 10 mm. There was no evidence of polyserositis or edema. The weight was 13.6 Kg.

May 1: The dog was in excellent condition. The venous pressure was 25 mm. The electrocardiogram showed a higher voltage and no slurring; it indicated a normal myocardial function.

Comment.—In this experiment generalized adhesive pericarditis and thickening of the pericardium occurred. This was followed by the development of polyserositis and subcutaneous edema (fig. 12). The venous pressure rose from 0 to 190 mm. and the cardiac output per minute fell to 1,107 cc. As soon as the pericardium was separated from the heart, a striking improvement in the circulation took place. The heart seemed to dilate as it was freed. It filled better, and it beat more forcibly. Following the operation all evidence of decompensation disappeared. Diuresis took place; the subcutaneous edema and the fluid

in the chest and the abdomen disappeared. The venous pressure fell to 25 mm. The cardiac output per minute rose to 3,528 cc. The general condition of the dog on May 1, 1930, was excellent (fig. 13). As far as could be determined, the dog showed no circulatory abnormality. There was no evidence of epicardial scar formation, no fixation of the heart, no adhesions to surrounding structures and no myocardial involvement.

COMMENT ON THE EXPERIMENTS

The essential factor in the production of Pick's disease, as can be seen from the experiments, is fibrosis and contracture of the parietal pericardium or epicardium, or both, forming a casing of scar which compresses the heart and primarily obstructs its filling, interfering with cardiac motion as a tightly fitting glove impairs the free movement of the hand. Generalized adhesions between the epicardium and the parietal pericardium are not sufficient in themselves to produce polyserositis. Such adhesions can be produced experimentally, and similar conditions are found clinically in which polyserositis does not develop. Nor is the presence of generalized adhesions necessary for the development of polyserositis. A marked degree of polyserositis developed in one experiment in which there were no adhesions to the heart.

Coincidentally with the development and contracture of scar tissue about the heart, the clinical manifestations of the Pick syndrome in the order of their appearance are: (1) a rise in the venous pressure, (2) ascites and the development of a fibrinous exudate on the liver, (3) hydrothorax and (4) pulmonary and subcutaneous edema. Subcutaneous edema and pulmonary edema are late manifestations of this disorder experimentally, as has been observed clinically. The mechanism in the formation of the fibrinous exudate on the surface of the liver is obscure. If the development of the syndrome had taken place over a sufficiently long period of time, the classic "Zuckergussleber" might have resulted (figs. 4 and 5). Together with the observations reported, there occurred general weakness and listlessness, a small and rapid pulse, cyanosis and a decrease in the minute volume output of the heart. It was shown roentgenographically that the heart and pericardium actually decreased in size and assumed a globular shape as the syndrome developed; after the pericardium was resected, the heart assumed its previous size and shape. Not infrequently the compression effect of the tight scar on the heart can be demonstrated fluoroscopically by the limitation of the systolic and diastolic movements of the heart.

The shift of the electrical axis of the heart with a change of position was of slight diagnostic significance in the experiments. Probably owing to the great mobility of the heart and pericardium in the dog,

a shift of the electrical axis was found even when the pericardium was markedly scarred. In those experiments in which there was no shift of the axis, the heart was securely immobilized by extrapericardial adhesions. Undoubtedly, the shift of the electrical axis of the heart is of greater diagnostic value in the determination of extrapericardial adhesions, a condition that is different in both its pathologic physiology and its therapy.

In tapping the ventricles for specimens of blood for cardiac output determinations, it was noted that the aspirating needle encountered a definite resistance if the parietal pericardium was thickened and scarred. We hesitate to recommend sticking the pericardium as a diagnostic aid because of the possibility of inflicting an injury to coronary vessels with the needle. In cases in which the diagnosis is obscure, however, may it not be useful as a clinical diagnostic aid?

On the basis of experiment it was found that the venous pressure was the most reliable index to the development of this condition. A rise in venous pressure was always noted before ascites or fluid in the chest could be demonstrated. Further experimentation is being undertaken to determine whether localized pericarditis, as for instance, involvement over only the left ventricle, results in the same sequence of events. A description of localized pericarditis will be reserved for a subsequent publication.

The casing of scar can almost always be resected. Usually a plane of cleavage can be found and separation can be carried out by blunt dissection. This was possible technically in every experiment except one. The exception represents a small percentage of clinical cases in which the scar so intimately involves the coronary vessels and the myocardium that its removal would involve a great hazard.

An important observation brought out in the experimental work was the necessity of excising the scar as completely as possible. Especially necessary was the excision of the scar from the region where the venae cavae enter the heart. At operation the incision in the thoracic wall should be such as to provide exposure of the lateral aspect of the right ventricle and right auricle, as well as of the left side of the heart.

In every experiment in which the pericardial scar was removed successfully a marked improvement in the circulation took place. It was always noted that as the heart was liberated from its encasement of scar an immediate dilatation of the heart occurred. It seemed as though the heart filled better and an immediate improvement in the circulation took place. That the heart returned to its normal shape and size after resection of the pericardium was shown roentgenographically. Following the resection of the scarred pericardium, the venous pressure

fell to the normal level. Diuresis took place, and ascites, hydrothorax and edema of the lungs and subcutaneous tissues disappeared. The minute volume output of the heart came back to the normal level. The dog became active and appeared normal in every respect. This improvement almost always seemed to be permanent. In only one experiment did an epicardial scar form after resection of the scarred parietal pericardium and again produce polyserositis. It would have been possible, however, to have resected this epicardial scar after it had formed. The experiments were conducted for several months following pericardiectomy, and as far as could be determined, the operation seemed to be completely curative. The experiments in which the pericardium had been resected did not show any adhesions between the heart and adjacent structures developing subsequently.

REPORT OF A CASE

A white boy, aged 14, was admitted to the Lakeside Hospital, on Sept. 4, 1929, with pain in the upper part of the abdomen, dyspnea on exertion and weakness.

The parents were of Slovakian stock; both were living. The father had been admitted several times to the psychopathic department of a local hospital, where the diagnosis of manic-depressive psychosis and alcoholism was made. The mother had had exophthalmic goiter and had undergone a partial thyroidectomy in 1925. There was one sister, aged 18 years, who was emotionally unstable but of normal mentality.

The history obtainable from the patient and his family was not accurate. He was born in Cleveland. He had had measles, mumps, pertussis and chickenpox in childhood. Later, he had frequent attacks of sore throat and infection of the upper respiratory tract. A tonsillectomy was performed in 1921 because of these frequent infections. There was no history of acute rheumatic fever, pain in the joints or chorea. At the age of 6, he appeared mentally deficient, and at 11, after several trials at school, he was sent to a state institution for the feebleminded. The intelligence quotients determined by various psychometric tests from 1922 to 1927 varied from 55 to 71 per cent. He was at home for two months in the summer of 1928; at that time he became short of breath on exertion and was easily fatigued. There was no history of any febrile illness or ascites at that time. He was then sent to another institution, where he remained until May, 1929. When he returned home he was short of breath and jaundiced, and complained of vague epigastric pain with occasional attacks of nausea and vomiting. His cheeks, ears and lips were dusky. His condition improved in the course of a month, but in July, 1929, he came to the Lakeside Hospital Dispensary complaining of shortness of breath. There was no jaundice or fever at that time. In August, according to the history obtained from the mother and sister, there was another attack of jaundice with light stools, dark urine, vague pain in the upper part of the abdomen and cyanosis. When he appeared at the dispensary, jaundice was not present.

He was then admitted to the medical ward. He appeared to be fairly well nourished but of obviously low mentality. Moderate orthopnea and cyanosis of the lips and cheeks were present. Throughout the period in the hospital the

temperature was normal. The pulse rate varied from 92 to 120 per minute and the respiratory rate from 24 to 48. The contour of the head was not remarkable, and there were no gross abnormalities of the eyes, ears or nose. There were a few carious teeth, and lymphoid tissue was present in both tonsillar fossae. The external jugular veins were abnormally distended. The thyroid gland was of normal size and consistency. There were no enlarged cervical glands, no tracheal tug and no thrill or bruit in the neck.

The thorax was symmetrical, and its movements were equal on each side. The costal flare appeared to be somewhat restricted, probably on account of the distention of the abdomen. The lungs were clear to percussion and auscultation. The bases were at the ninth rib with excursion of less than one interspace on deep inspiration. No fluid was demonstrable in the pleural cavities. There was no abnormal precordial pulsation or retraction and no Broadbent sign. The

Fig. 14.—Patient before pericardiectomy.

cardiac apex was in the fifth intercostal space at the midclavicular line; the right border of cardiac dulness was beneath the sternum and the upper border was in the third interspace. The cardiac sounds were normal. There was no thrill, friction rub or murmur. A marked pulsus paradoxus was present. The pulse pressure was low; the blood pressure was 106 systolic and 78 diastolic. The abdomen was markedly distended (fig. 14). Shifting dulness and a fluid wave could be elicited. The edge of the liver extended to the umbilicus. It was smooth, firm and slightly tender. The spleen was enlarged and firm. The genitalia, reflexes and extremities were normal.

September 13: Stereoscopic films of the chest showed the right apex to be more cloudy than the left and the left lung field to be better illuminated than the right. There was some increase in the hilar markings on both sides, with an increase in the bronchial markings along the right border of the cardiac shadow. There was some thickening of the interlobar septum on the right. The dia-

phragms were fairly smooth and the costophrenic sinuses were clear. The shadow of the heart seemed slightly enlarged. The appearance suggested a slightly thickened pleura over the right side of the chest. The diaphragms appeared of about normal height. There was no evidence of a high diaphragm on either side.

September 20: Fluoroscopic examination of the chest and mediastinum showed the lung fields to be clear and the cardiac shadow slightly enlarged toward the left. The posterior mediastinum was clear, the diaphragms smooth and the costophrenic sinuses clear. There was no definite evidence of mediastinal tumor.

Electrocardiograms were taken with the patient in the dorsal position and also with the patient on the right side. Dr. R. D. Leas reported that the voltage

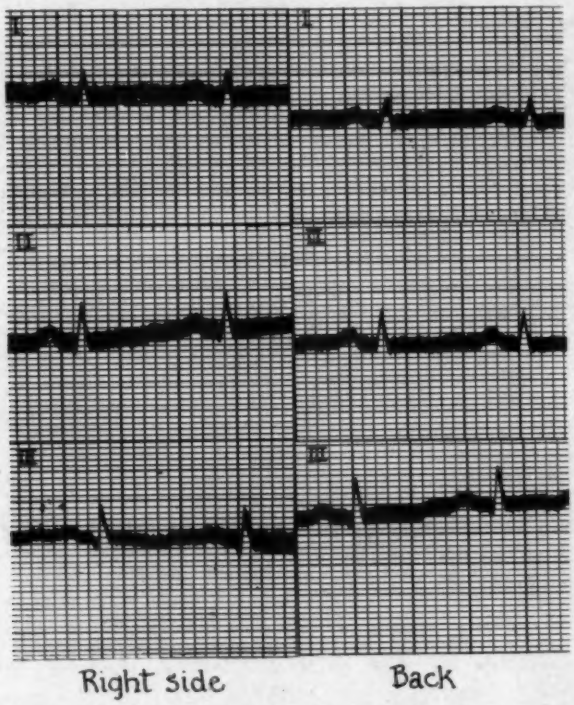

Fig. 15 (September 20).—Low voltage and slurring of Q R S complex with no shift of the electrical axis on change of position.

was below normal and that there was slurring of the Q R S complex in all leads. No shift of the electrical axis was noted with change in position (fig. 15).

The urine was straw-colored and acid, with a specific gravity of 1.014. It did not contain albumin, sugar or cells. A few hyaline casts were found on one examination. The Gmelin test was negative for bile pigments. The Wassermann reaction of the blood was negative. Examination showed: red blood cells, 6,680,000; white blood cells, 7,750; hemoglobin, 85 per cent; polymorphonuclear leukocytes, 62.5 per cent; lymphocytes, 27.5 per cent, and mononuclear cells, 10 per cent. The icteric index, fragility test of the red blood cells and platelet count were normal. The clotting time was six and one-half minutes and the bleeding time one and one-half minutes.

Abdominal paracentesis yielded 650 cc. of clear brownish fluid which did not clot on standing. It had a specific gravity of 1.020 and a cell count of 400 per cubic millimeter.

Except for some reaccumulation of fluid in the abdomen, there was little change in the patient's condition during the period in the hospital. He was kept in bed for several weeks, and was then allowed to be up and about the ward. We saw the patient on the medical ward soon after his admission, and from our experience with adhesive pericarditis in the laboratory we did not hesitate to make the diagnosis of Pick's disease. It was decided, however, to observe the condition over a longer period of time. The patient was therefore discharged from the hospital on October 5.

He was confined to his home. Although he was able to walk about the house, he had no desire to play with other boys. He developed a mild infection of the upper respiratory tract. Dyspnea became more marked. A troublesome cough developed and he was unable to lie recumbent in bed. He was readmitted to the hospital ten days after his discharge.

The patient had orthopnea. An unproductive cough was present. Cyanosis of the cheeks, ears, lips and finger-nails was conspicuous. The veins of the neck, arms and hands were distended. Dilatation of the retinal veins was present. The patient was weak, and he was kept in bed. Edema of the scrotum was present, but elsewhere there was no subcutaneous edema. While he was in the recumbent posture spasms of coughing developed, and he had to be propped up on pillows and a back rest to sleep. The temperature was normal. Pulsus paradoxus was present. The pulse rate varied from 100 to 110 and the respiratory rate from 28 to 40. The systolic blood pressure was from 90 to 100 and the diastolic blood pressure from 70 to 80.

Fluid was never demonstrated in the chest by clinical examination. At times scattered, coarse râles were heard. There was slight impairment of tactile fremitus below the angle of the scapula on each side, but the percussion note was unchanged. There was no precordial activity. The left border of the heart, as determined by percussion, was 10 cm. to the left of the midsternal line and the right border of the heart was 3.5 cm. to the right of the midsternal line. There was no detectable change in the position of the heart with change in position of the chest.

The abdomen was markedly distended with fluid. The liver was greatly enlarged, firm and slightly tender to pressure; the edge was at the level of the umbilicus. The spleen was large and firm.

October 21: A roentgenographic report by Dr. C. C. McCoy stated: "The film of the heart and the chest in the first oblique position shows evidence of a pleural reaction in the left costo-phrenic sinus which was not noted previously. There might be a small amount of fluid here. There is also a pleural reaction at the right costo-phrenic sinus which seems a little more marked than at the last examination." The measurements of the heart are seen in figure 16.

November 20: Dr. D. Steel made the following report of a fluoroscopic examination: "The cardiac silhouette is triangular in outline. The outlines of the various chambers are obliterated. The amplitude of pulsations is markedly reduced and almost obliterated. The heart is fixed. The respiratory excursion is nil. The retrocardiac space and the retrosternal space are definitely hazy. In the second oblique view the outline of the left ventricle remains posterior to the bi-diaphragmatic angle in all phases of respiration. The superior vena cava and the innominate vein are easily made out. Both hilus regions are definitely increased. Fluoroscopically no tenting of the diaphragms can be made out. The

inner half of the left diaphragm showed practically no motion. The findings suggest an adherent pericardium with changes in the retrosternal and retrocardiac spaces."

The laboratory observations were as follows: The urine contained a slight trace of albumin and an occasional granular cast. Examination of the blood showed: white blood cells, 8,000; red blood cells, 6,300,000, and hemoglobin, 105 per cent. The stained smear of the blood showed the cells and platelets to be normal. The percentages obtained in the differential cell count were: polymorphonuclear leukocytes, 70; lymphocytes, 20; mononuclears and transitionals, 6; eosinophils, 3, and basophils, 1. The vital capacity did not exceed 1,500 cc.; the calculated capacity was 2,700 cc. The venous pressure was determined by inserting an aspirating needle connected to a glass manometer tube containing physio-

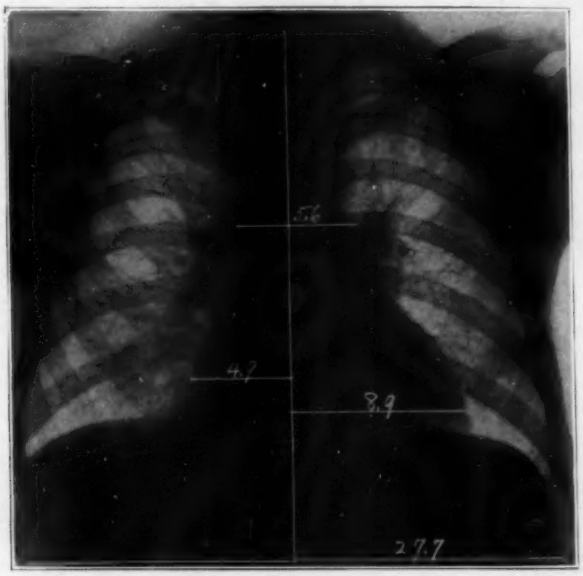

Fig. 16 (Oct. 21, 1929).—Six foot roentgenogram of the chest.

logic solution of sodium chloride into the median cephalic vein at the anterior level of the heart. The venous pressure measured 350 mm. of physiologic solution of sodium chloride. The normal venous pressure in the median cephalic vein, as quoted by Eyster,[7] is from 40 to 60 mm. of water with an upper limit of 110 mm. A cardiac function test was carried out, which consisted of having the patient walk up and down one flight of stairs four times. This exercise caused marked flushing of the face and shortness of breath. The systolic blood pressure rose from 100 to 130 and the diastolic pressure from 80 to 88. The pulse rate per minute rose from 94 to 120. The blood pressure and the pulse rate returned to their previous levels at the end of thirteen minutes.

Comment.—A boy, aged 13, presented symptoms of dyspnea on exertion and weakness of about one and one-half years' duration; these were insidious in onset and progressive. Several transient attacks of

jaundice and vague epigastric pain appeared during this period. There was no history of associated fever. There was no history of acute rheumatic fever or chorea. The patient had had frequent attacks of rhinitis and sore throat, and because of the latter the tonsils were removed in 1921. Aside from the mental retardation the patient presented the following symptoms: orthopnea, cyanosis, an increased venous pressure, a low pulse pressure, ascites with enlargement of the liver and spleen, edema of the scrotum, slight pulmonary edema, fixation of the heart and limitation of the diastolic excursion of the ventricles.

The diagnosis of concretio pericardii (Pick's disease) was made. The etiology was obscure. The picture presented by this patient was an exact duplication of the experiments in which intrapericardial adhesions were produced by surgical solution of chlorinated soda. The pathologic physiology of the condition was based on the impairment in the filling of the heart produced by a snugly fitting, thickened pericardium. Pericardiectomy was indicated.

Operation.—The patient was digitalized. The evening before operation, 300 cc. of blood was removed and this seemed to relieve some of the engorgement.

Nov. 21, 1929: Pericardiectomy was performed. The patient was placed in a semirecumbent position on the operating table and ether vapor anesthesia was administered. The incision was made from the costal margin in the midclavicular line on the left; it curved medially and superiorly to the midsternum, followed the midsternum for 2 inches (5.1 cm.) and then curved laterally to the midclavicular line at about the level of the third rib. The pectoralis major muscle was divided at the two lateral arms of the incision. The underlying costal cartilages, sternum and ribs were exposed. The soft structures were separated from the fourth, fifth and sixth costal cartilages and these were divided close to the sternum and at their junctions to the ribs. The mediastinal structures were separated from the sternum by blunt dissection with little difficulty. The sternum was removed by a rongeur over about three fourths of its width and 3 inches (7.6 cm.) of its length. The pleural sinus on the left was then dissected from the pericardium. The pleura was adherent to the pericardium, and this separation had to be carried out by sharp dissection (fig. 17). During this procedure the pleura was nicked in one or two places, but was promptly closed, protecting the pleural cavity from the entrance of air. The left phrenic nerve was not encountered; presumably it was dissected from the pericardium with the pleura. While the costal cartilages and part of the sternum were being resected, the pulse was irregular. The anesthetist thought that the cyanosis was a little more marked, but no change in the blood pressure or the pulse rate was recorded on the chart that he kept.

The pericardium was then incised over its midanterior portion. It was very thick and the incision was carried deeper and deeper until at one point it actually entered cardiac muscle. The scarred pericardium was incised for about 6 cm. (fig. 18) and a line of cleavage was found. Separation was carried out with the scalpel. This left a distinct layer of fibrous tissue on the heart, but as the separation proceeded laterally the epicardium seemed to be entirely free from scar. This separation of the pericardium from the heart was carried out laterally over the base and posteriorly by the index finger slowly and cautiously until the

entire surface of the heart was swept clean (fig. 19). During this procedure the pulse became irregular at times owing to extrasystoles, though it had seemed more disturbed a little while before, when the costal cartilages were being removed, than it did while the adhesions between the heart and pericardium were actually being separated. The left ventricle was freed before the right ventricle. It was apparent to every one who saw the operation that the heart actually dilated as it was being freed from the adhesions. The anesthetist repeatedly reported that the pulse had become stronger and that the pulse pressure had definitely increased.

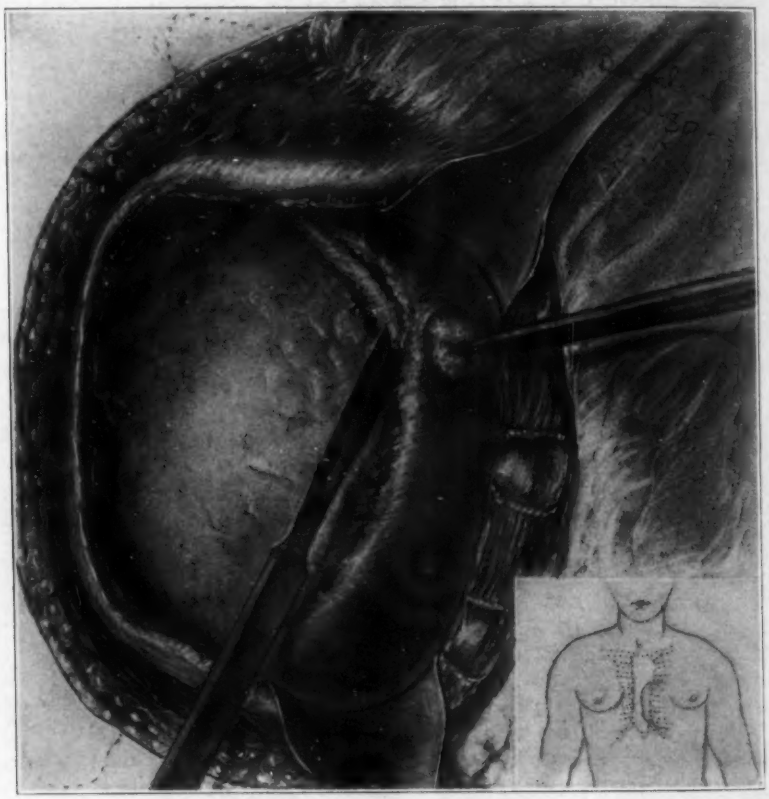

Fig. 17.—The fourth, fifth and sixth costal cartilages on the left side were resected and the sternum was partially resected. The pleural sinus on the left was dissected from the pericardium.

Lying over the surface of the heart anteriorly was a layer of white fibrous scar about 10 sq. cm. in area. This was picked up with forceps and removed from the heart with considerable difficulty. Here and there sharp dissection from the ventricle was carried out. After this scar tissue was removed, the anterior coronary vessels could be seen. The surface of the ventricles and the auricles now seemed to be free from scar tissue. The pericardium was 4 or 5 mm. thick. It was incised over the base, and the right margin of the pericardium was grasped

Fig. 18.—The pericardium was incised over the left ventricle. It was difficult to determine the plane of demarcation between scar and myocardium.

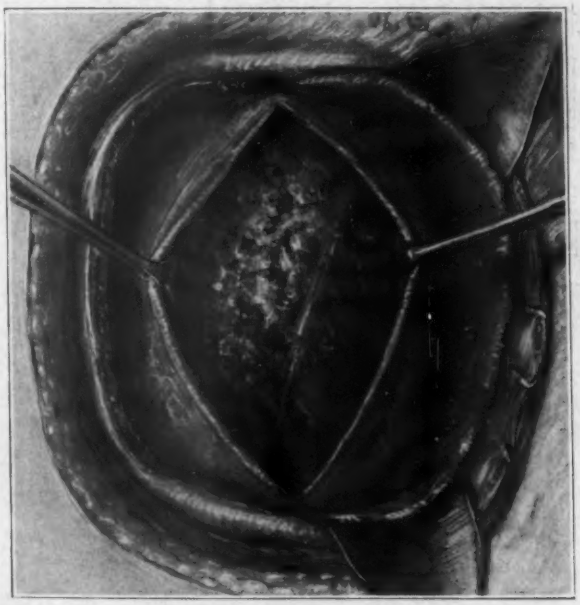

Fig. 19.—A plane of cleavage was found and separation was carried out by blunt dissection. The heart seemed to bulge through the opening in the scar as the separation progressed.

with Allis forceps and drawn to the left. This brought into view the right pleural sinus. The latter was dissected from the pericardium well around to the right (fig. 20). The exposure of this region, however, was inadequate. The venae cavae could not be seen. Excision was now carried out. The pericardium on the right and over the base of the heart was removed, but excision here was hazardous because we could not see or identify the venae cavae. Excision on the left side was carried well down to the emergence of the pulmonary vessels. The excision of the pericardium was complete except for an area posterior to the heart and a small area over the right auricle where the venae cavae entered the pericardium and where the exposure of the structures was inadequate (fig. 21). There was some oozing of blood from the surface of the heart posteriorly, but this was not marked.

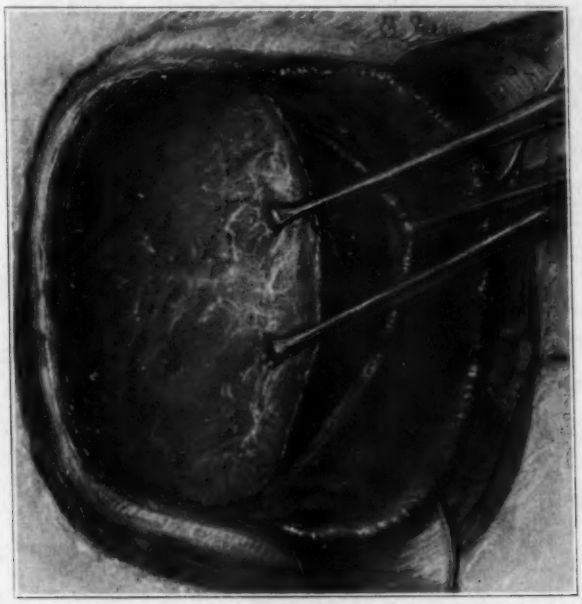

Fig. 20.—The pericardium over the right side of the heart was drawn to the left. The right pleural sinus was dissected from the pericardium.

The bony framework over the anterior surface of the heart had been almost completely removed by the resection of the cartilages and of part of the sternum. The flap of soft parts was then placed in its bed, the covering of the heart and the pleura on the left being the inner surface of this flap. The soft parts were sutured with two layers of silk and the skin was closed with silk. A small drain was placed in the wound to allow for extravasation of fluid or blood and to prevent cardiac tamponade. The wound was sealed wtih silver foil and covered with a voluminous dressing.

The excised pericardium is shown in figure 22. Examination by the pathologist yielded the following observations: The fragments of tissue varied in thickness from 1 to 6 mm. One surface of each was granular and well vascularized and the other surface was dense and smooth. The denser surface of

Fig. 21.—The pericardium was excised as was also a plaque of epicardial scar lying over the left ventricle. The coronary vessels stand out well.

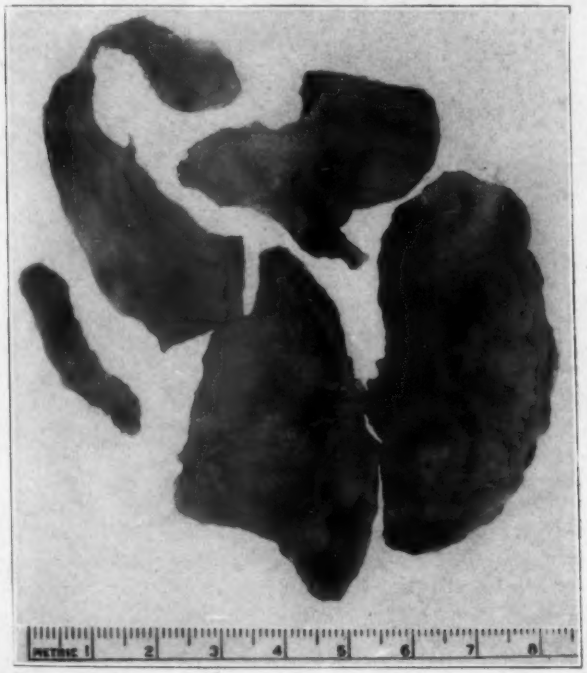

Fig. 22.—The portion of the pericardium excised at operation. It varied in thickness from 1 to 6 mm. Microscopically, this structure closely resembled the scar produced experimentally.

one of the specimens contained a small, round, hyaline plaque. Sections through the fragments were essentially similar and showed a dense fibrous tissue which was cicatricial. One side of each section was very dense; the fibers were arranged parallel to one another, for the most part, and there was extensive hyalinization. As the other surface was approached, the tissue became looser and contained many small blood vessels and, in places, lymphocytic infiltration. At the extreme outer edge of some of the fragments there were clusters of fat cells. The hyalinization was not uniform and small hyaline plaques often showed a dense peripheral zone of lymphocytic infiltration. The diagnosis was given as chronic inflammation with hyalinization of fibrous connective tissue.

It was the opinion of every one who observed the patient that the cyanosis of the face and lips was less marked at the end of the operation than before it began, and that the dilatation of the jugular veins was less marked. The blood

Fig. 23 (Dec. 23, 1929).—Six foot roentgenogram of the chest.

pressure was 100 systolic and 56 diastolic. The pulse pressure was doubled by the operation. This meant that the heart was filling better and expelling more blood per beat. The pulse rate per minute was about 140. Within a few minutes after the anesthesia was stopped, the patient regained consciousness. At midnight after the operation, the blood pressure was 114 systolic and 70 diastolic. The cyanosis of the lips had almost completely disappeared. Twenty-four hours after operation the blood pressure was 110 systolic and 70 diastolic and the cyanosis of the lips had completely disappeared. The respiratory rate per minute was about 40; the respiratory movements were shallow; the pulse rate per minute was 120 and the temperature 37.8 C. (100 F.). Later in the day the temperature rose to 39.5 C. (102.9 F.), and the patient had a troublesome cough with expectoration of thick tenacious mucus. The respiratory rate per minute at that time was 30, the pulse rate 120 and the blood pressure 100 systolic and 60 diastolic. An occasional small dose of morphia relieved the pain incident to coughing. The temperature diminished in a few days and the cough disappeared.

The drain was removed at the end of twenty-four hours; the bloody serous discharge, which had been profuse at first, quickly diminished. The sutures were removed on the fifth day, and the wound was completely closed by the seventh. The patient was allowed out of bed on the fourteenth day. On the eighteenth day the venous pressure was 200 mm. of water, the reading having been taken exactly as before. The vital capacity was about 1,150 cc. The blood pressure was 110 systolic and 70 diastolic.

December 23: A roentgenologic report by Dr. D. Steel stated: "Compared to the previous measurements, the transverse diameter of the heart has decreased. This was due, apparently, to a decrease in the left median distance (fig. 23).

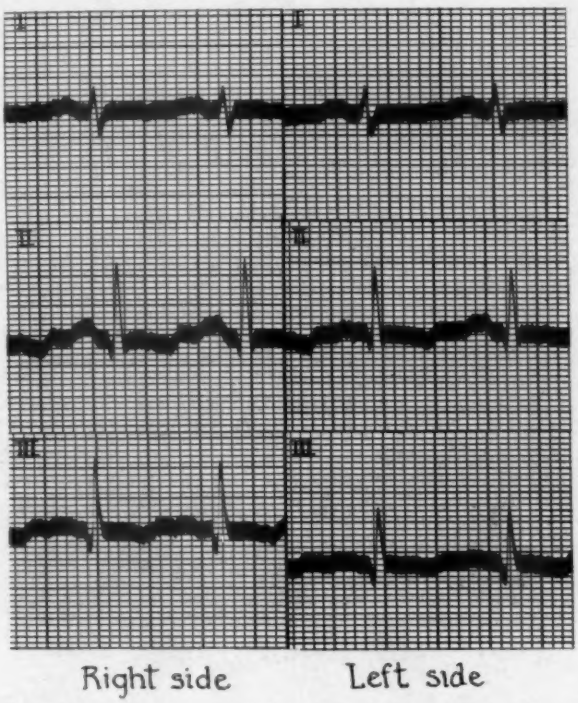

Fig. 24 (December 24).—A slight degree of right ventricular preponderance, with an increase of voltage, less slurring of the Q R S complex and no shift of the electrical axis on change of position.

The median half of the left diaphragm was immobile. As far as can be made out fluoroscopically, the heart does not move upward with respiration. The amplitude of the pulsation has definitely increased since the previous examination."

December 24: An electrocardiographic report by Dr. R. D. Leas stated that the patient had received 12 cc. of tincture of digitalis on November 19 and 20, and 8 cc. on November 23. There was a slight degree of right ventricular preponderance with an increase of voltage and less slurring of the Q R S complex. There was no evidence of a shift of the electrical axis with change in position (fig. 24).

The patient was discharged from the hospital on December 30. By diuresis he had lost 4 Kg. since operation (fig. 25). The fluid had completely disappeared from the abdomen. Edema of the scrotum disappeared, as did also the râles in the lungs, the cough and the orthopnea. The patient was up and about the wards without dyspnea; his activities frequently had to be restrained by the nurses. The liver and spleen had not changed in size. At times the slightest trace of cyanosis of the lips was noticeable; at other times cyanosis was absent. The jugular veins were dilated, but the degree of dilatation was considerably less since operation. The venous pressure was 190 mm. of water. The blood pressure was 114 systolic and 68 diastolic. The vital capacity was 1,850 cc. The red blood cell count was 5,090,000 and the hemoglobin content 80 per cent. The occasional cast and the trace of albumin found in the urine before operation had disappeared.

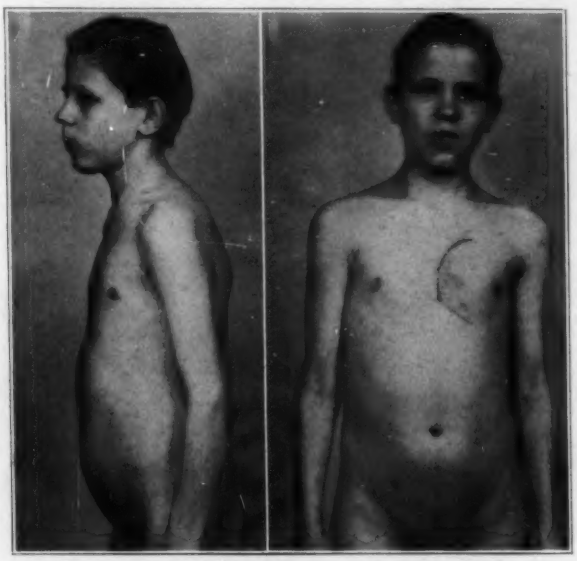

Fig. 25.—Patient after pericardiectomy.

A week later, he could walk upstairs without dyspnea, but he was a little short of breath on running. After climbing the stairs his pulse rate per minute was 104 and his blood pressure 118 systolic and 68 diastolic. The jugular veins were not distended, and there was no cyanosis, cough, edema, ascites or fluid in the chest. The margin of the liver was one fingerbreadth above the umbilicus. There was marked precordial pulsation but no murmur and no pain over the precordium.

Jan. 20, 1930: The blood pressure was 118 systolic and 70 diastolic; the venous pressure was 210 mm. of water and the vital capacity 2,100 cc. Two weeks later, he could run up a short flight of stairs without dyspnea. The pulse rate per minute was 102; the blood pressure was 124 systolic and 82 diastolic. The venous pressure, taken indirectly by means of the water manometer of Eyster, was 170 mm. The edge of the liver was halfway between the costal margin and the umbilicus in the midline. The spleen had decreased in size but was still palpable. The vital capacity was 2,400 cc.

February 20: The patient was very active. The pulse rate per minute was 96; the blood pressure was 122 systolic and 76 diastolic. The veins in the neck were not distended. There was probably the slightest tinge of color to the lips but none to the ears. The vital capacity was 2,300 cc. The liver was still enlarged, but there was no fluid in the abdomen and no edema.

March 19: There was some pulsation in the veins of the neck but no cyanosis. The venous pressure, obtained by the direct method, was 17 cm. of water. The vital capacity was 2,800 cc. The blood pressure was 120 systolic and 65 diastolic.

March 19: A roentgenogram of the chest showed the heart lying in a more vertical position than before operation (fig. 26). The transverse diameter of the heart was less, but this was probably due to the position now occupied by the heart. The diaphragm was smooth and regular and was lower than at the previous examination. The costophrenic sinuses were clear. There was no evi-

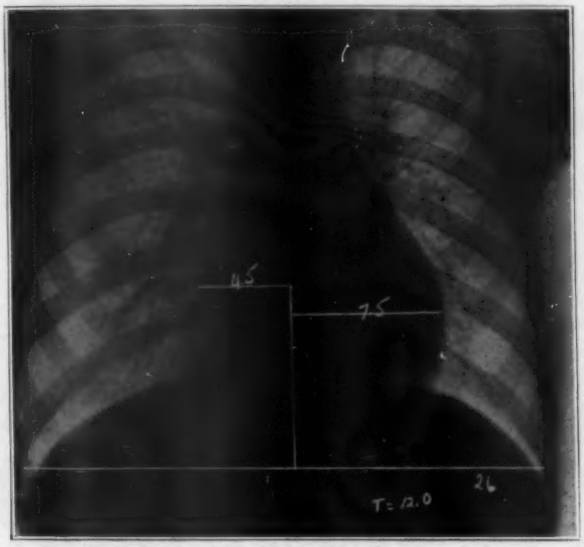

Fig. 26 (March 19, 1930).—Six foot roentgenogram of the chest.

dence of fluid at the base of either lung. Fluoroscopically, the pulsation of the left ventricle was normal. The pulsation of the right side, however, seemed to be less than normal.

An electrocardiographic report by Dr. Leas showed that the same degree of preponderance of the right ventricle was noted as when the previous records were made. The voltage had increased more than in the previous record. The slurring of Q R S had disappeared, except in lead 1, where it was slight. The progressive increase of voltage and lessening of the slurring first noted in Q R S suggested an improvement in the condition of the myocardium (fig. 27).

The sister believed that the patient was brighter and a little more alert mentally. As we recognized that an improvement in the cerebral circulation might bring about this result, further intelligence tests were carried out. The results, however, gave an intelligence quotient of 45. This was less than the result obtained in 1927, but it is altogether probable that at that time the circulatory condition was not impaired.

Comment.—The diagnosis of adhesive pericarditis (Pick's syndrome) was confirmed at operation. The pericardium was exposed by removal of the left fourth, fifth and sixth costal cartilages and part of the sternum. The pleura was dissected from the pericardium on each side. The pericardium was thickened and everywhere adherent to the heart. The separation of the pericardium from the heart was carried out by sharp dissection over a small area of the ventricles anteriorly; elsewhere the separation was carried out by blunt dissection. The

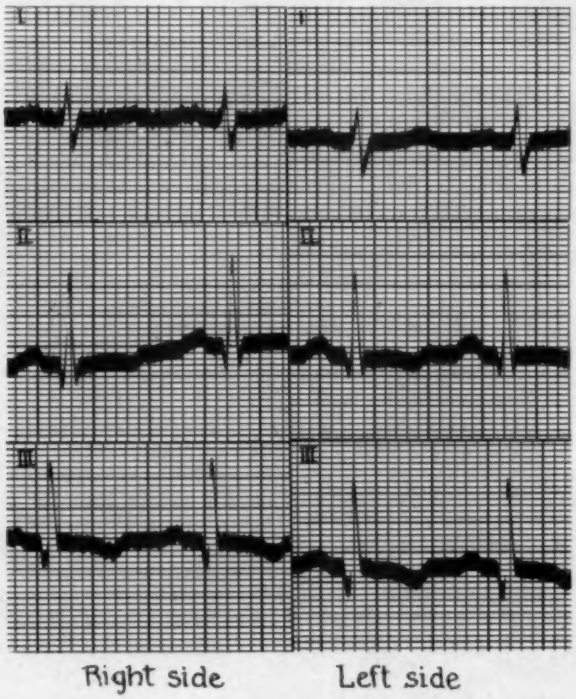

Fig. 27 (March 19, 1930).—A slight degree of right ventricular preponderance, further increase of voltage, disappearance of slurring of the Q R S complex except in lead 1 where it was slight. These observations suggest a progressive improvement in the condition of the myocardium.

exposure of the right side of the heart was inadequate; the venae cavae could not be seen. The pericardium was excised completely except over a small area posteriorly and to the right where the venae cavae entered the pericardium. A small drain was placed in the wound as a precaution against cardiac tamponade, and the wound was sutured.

The improvement was dramatic. As the heart was liberated from its encasement of scar, it definitely dilated, and the anesthetist reported improvement in the condition of the patient. The systolic pressure

rose, and the pulse pressure increased. At the close of the operation the cyanosis of the face, which was conspicuous before operation, had almost completely disappeared. The jugular veins were less distended.

Diuresis subsequently occurred, the patient losing 4 Kg. of fluid. The ascites and the edema of the scrotum and lungs completely disappeared. The vital capacity rose from 55 per cent to normal. Orthopnea

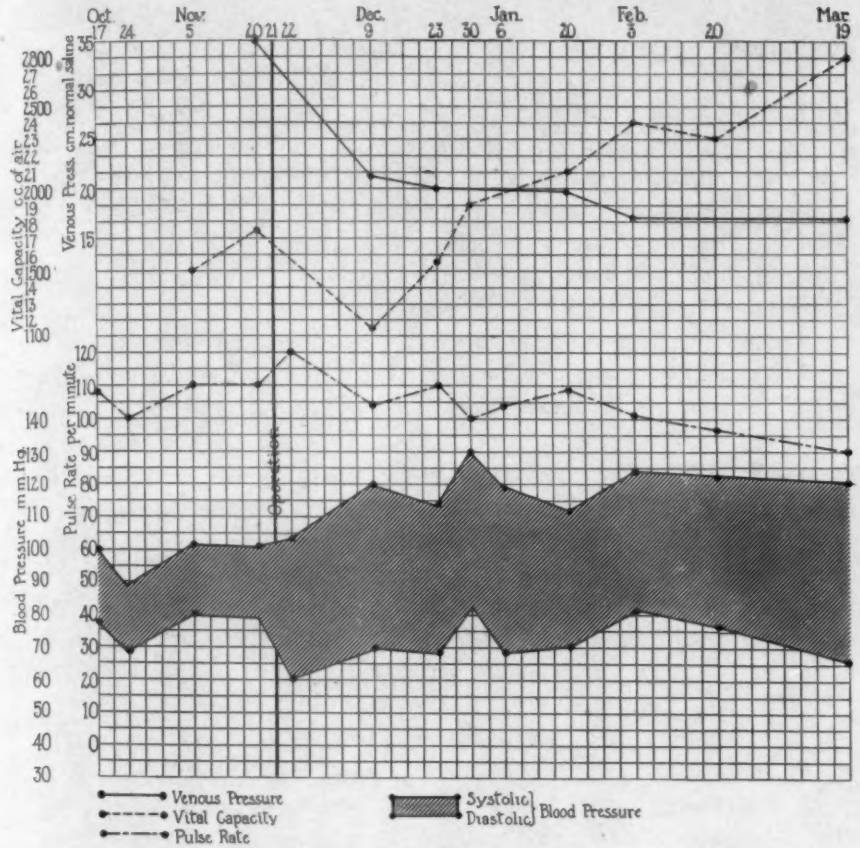

Fig. 28.—Venous pressure, arterial pressure, pulse rate per minute and vital capacity represented graphically before and after pericardiectomy. The shaded area represents the pulse pressure.

completely disappeared. The systolic pressure rose 15 to 20 mm. The pulse pressure doubled. The venous pressure, as determined by the direct method, fell from 350 mm. of physiologic solution of sodium chloride before operation to 170 mm. after operation (fig. 28).

During the first few months after operation the patient led an active life at home. He could run up one flight of stairs without dyspnea,

but the response to exercise had not fully returned to normal. On Oct. 3, 1930, he appeared like a normal boy. His weight was 120 pounds (9 Kg.) and his height was 64 inches (162 cm.). He was strong and active. He could jump fences, got into numerous fights with playmates of his own age and was able to take care of himself. The blood pressure was normal, but the pulse rate was 110 per minute. The patient, however, was a little excited in contemplation of a venipuncture which was about to be done. The venous pressure was 150 mm., taken in the cephalic vein of the arm. There was no cyanosis. The liver and the spleen were no longer palpable. There was no water in the abdomen or chest.

It will be recalled that the operation did not provide exposure of the right auricle where the venae cavae entered the pericardium. The pericardium was dissected free from this area by blunt dissection, but it could not be excised close to these vessels. The removal of the pericardium over this area, therefore, was incomplete. In view of our experience in experiment 8, we question whether or not the limitation of the movement of the right side of the heart, as seen fluoroscopically, and the slightly increased venous pressure may not have been due to a small segment of pericardium still remaining over this region.

BILATERAL EXPOSURE FOR THE RESECTION OF THE PERICARDIUM

As far as could be determined from the literature, the Duval-Barasty incision is the only one that provides an extensive exposure of the heart. Every aspect of the organ can be approached through this exposure. In his operation for the relief of mitral stenosis Cutler had used this incision in six cases; with this experience as a background, he felt that probably this exposure was too shocking to the patient, who was seriously decompensated.

The following is a description of a new incision that seems to be especially applicable to pericardial surgery. It provides a bilateral exposure of the heart without splitting the sternum, without entering the pleural spaces and with a minimal impairment of the respiratory mechanism.

It consists of an H-shaped incision, with the cross-bar of the H extending over the midline of the sternum and the parallel arms of the H placed at the level of the third costal cartilage above and at the junction of the manubrium with the sternum below (fig. 29). The transverse incisions extend laterally from the midsternal incision for about 5 cm. in each direction. The midline incision is carried to the sternum. The upper transverse incision transects the pectoralis major muscle for a short distance at its origin from the sternum. The two

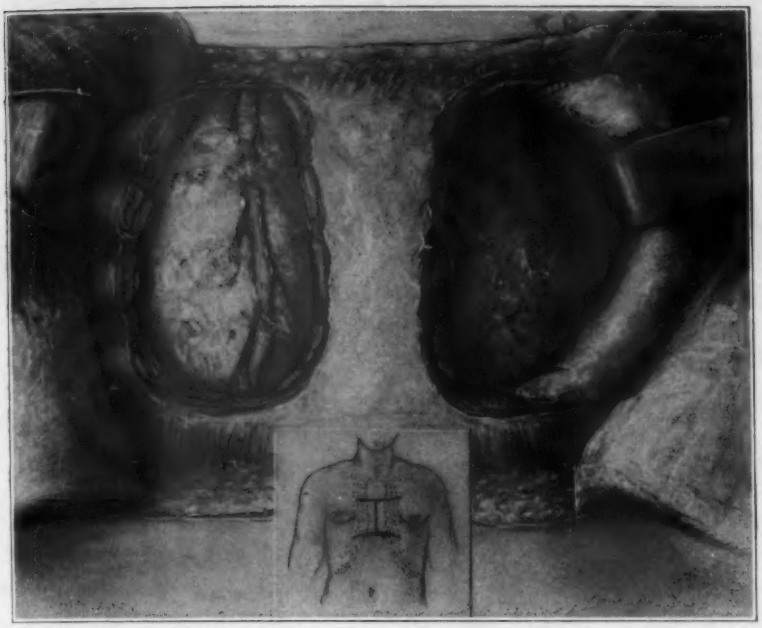

Fig. 29.—A new exposure for resection of the pericardium. The pleural cavities are not entered. The sternum and the lowest costal cartilages are not disturbed. The mechanics of respiration are thereby little impaired.

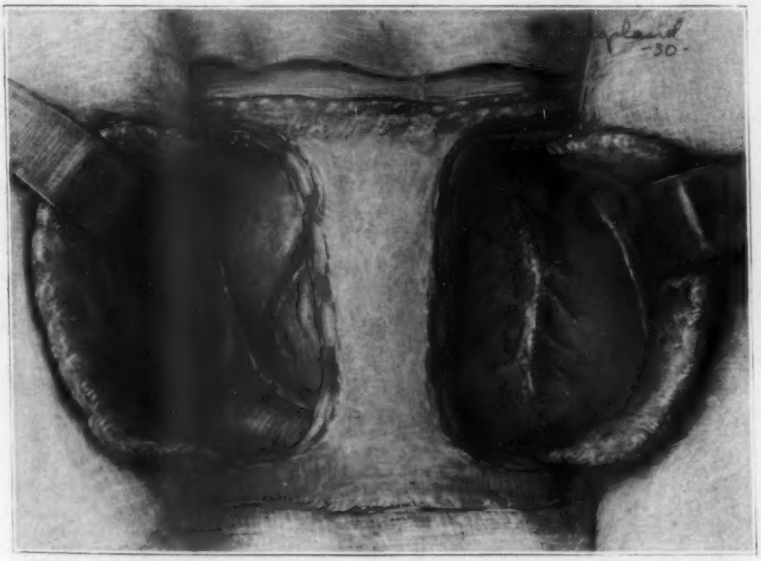

Fig. 30.—A new exposure for resection of the pericardium. A wide exposure on each side of the heart is provided.

flaps of soft parts thus made are dissected laterally to expose the sternum and the costal cartilages. The third, fourth, fifth and sixth costal cartilages on each side of the sternum are resected. The internal mammary vessels are ligated. The pleural sinus is dissected from the pericardium on each side, and this provides an excellent exposure well around laterally on each side of the pericardium. The left phrenic nerve should be dissected from the pericardium with the mediastinal pleura. The right phrenic nerve may or may not be seen along the superior vena cava. The pulmonary vessels can be seen on each side. An almost complete resection of the pericardium can be carried out, leaving only the portion posterior to the heart (fig. 30).

The sternum is not disturbed. So that the movements of the diaphragm are not impaired, the seventh costal cartilage should not be resected. The flaps of soft parts are reapproximated.

We have not as yet used this exposure on a patient. The flaps are so short that we would not anticipate any disturbance to healing, from interference with the blood supply, even in the corners of the flaps.

COMMENT AND SUMMARY

A form of cardiac decompensation, consisting primarily of scarring and contracture of the parietal pericardium, usually but not always accompanied by intrapericardial adhesions and consisting secondarily of polyserositis, the formation of a fibrinous exudate or scar tissue on the liver and sometimes subcutaneous and pulmonary edema—a syndrome described by Pick and bearing his name—is highly amenable to surgical therapy. Unfortunately, surgical measures have had altogether too little application in the treatment for this condition. With few exceptions, internist and surgeon alike are unacquainted with the pathologic physiology underlying the condition and its relief by pericardiectomy.

A method for the production of this disorder experimentally is described. It consists of the application of surgical solution of chlorinated soda in the pericardial cavity. The introduction of this solution results in generalized intrapericardial adhesions, thickening and fibrosis of the parietal pericardium and sometimes of the epicardium, ascites, fluid in the chest, enlargement of the liver, together with a fibrinous exudate on the liver, and sometimes pulmonary and subcutaneous edema.

Observations on the experimental production of the Pick syndrome and its relief by pericardiectomy are presented.

Observations on a clinical case of the Pick syndrome and its relief by pericardiectomy are given.

It is hoped that the production of this syndrome in the laboratory will provide further experiences for both internist and surgeon that may have direct application both in the recognition of the condition and in its therapy. To us, these experiments have been highly beneficial. They not only gave us more confidence in making the diagnosis, but they furnished a background of experience that was invaluable for the performance of the operation on the human being.

A new exposure for the resection of the pericardium is presented.

ABSTRACT OF DISCUSSION

DR. LEO ELOESSER, San Francisco: I should not like to let Dr. Beck's remarkable piece of work go without a word. Last year in an operation on a Chinese child about 4 years of age, I went through a pericardium so extraordinarily thick that I did not know whether I was dealing with pericardium or myocardium until, slowly proceeding, I fortunately found a small, free pericardial cavity. The pericardium was fully half an inch thick, and there were some tender adhesions between it and the myocardium, yet they could be readily separated.

To my dissappointment I found, after resecting the pericardium, that it was tuberculous. The child, after making a temporary recovery, died about three or four months afterward of tuberculous meningitis.

DR. HOWARD LILIENTHAL, New York: I am always thrilled when I hear a presentation such as we have just had by Dr. Beck. I have wanted cases such as these, but I have had the greatest difficulty in persuading our physicians to turn them over to me. Dr. Groedel of Bad Nauheim happened to be coming to this country at the same time that a patient of his with Pick's disease and calcified pericardium came over. He turned the patient over to me, and I operated on her. She was a woman in the early twenties with enormous ascites, slight hydrothorax on each side, edema of the legs and feet and acutely ill. I believe that I have reported this case before, or, at least, have mentioned it here. My only reason for speaking of it now is that in this patient, whose condition was almost as bad as it could be, I made the Duval-Barasty incision with satisfactory results. If the incision is made almost to the umbilicus, cutting straight through the diaphragm and the center of the sternum with Shoemaker's sternum shears, it is astonishing to see what an enormous exposure of the pericardium will be effected.

Dr. Groedel's patient was relieved by what I did for her and was able to leave the hospital, although I found that the pericardium had literally turned to stone. I did the best I could to get into it from the apex upward, but I found that it was quite impossible, so I made an incision at what seemed to be a less dangerous place toward the base of the heart and opened directly into the auricle. I was naturally alarmed and packed the pericardial wound with gauze. In spite of the complications including a slight infection, the woman was able to be up and around two or three weeks after the operation and left the hospital "improved," even with so little freeing of a comparatively unimportant part of the heart, the auricle. Something caused the improvement of that patient. I cannot believe that it was the splitting of the sternum, because of the calcified pericardium. The roentgenogram had demonstrated that before the operation, but then I thought that the pericardium would be like a nutshell that I could break and peel open as one would an almond from the kernel.

My only reason for inflicting this history on you now is in the hope that Dr. Beck will not do the operation which he has cleverly enough devised and which involves cutting the ribs on both sides of the sternum. I believe that the Duval-Barasty incision is not conducive to postoperative shock from what I was able to observe in this one, but very difficult and dangerous, case. I do not believe that this operation would be as dangerous ultimately as to operate on both sides of the sternum, with the danger of entering both pleural cavities, or one at any rate.

I would suggest also that in this operation an anesthetic should be ready for intrapharyngeal hyperpressure.

DR. E. D. CHURCHILL, Boston: I have been impressed by Dr. Beck's well rounded presentation of a clinical case supplemented by careful experimental work.

There are many interesting problems presented by an adherent heart. I believe that the adhesions between the two layers of the pericardium are the least important in the production of symptoms. On the basis of one case that came to autopsy I can confirm the experimental observation of Dr. Beck that cardiac decompensation can occur without there being any adhesions between the two layers of the pericardium. In the case mentioned the outer layer of the pericardium was drawn laterally and fixed to a scarred area of tuberculosis in the lung. The patient died showing the signs and symptoms of cardiac decompensation with tremendous dilatation and hypertrophy of the heart. Autopsy revealed no valvular disease and no adhesions between the layers of the pericardium.

I think that it must be accepted that the adherent heart is a mechanically disabled one and that this disability need not always be evident clinically. I cannot believe it to be a coincidence that Pick's disease is frequently referred to as "ascites praecox." It seems to be characteristic for the symptoms to occur at this age, the age at which the rapid growth of the body with increasing metabolic needs requires an increased cardiac output. The heart fails to meet this demand because it is unable to increase its diastolic filling, owing to the throttling scar. I have under observation a physician from Nova Scotia who had acute pericarditis in 1897 when he was a student at Johns Hopkins University. He settled in Nova Scotia, carried on the active life of a general practitioner and only recently broke down when, superimposed on his mechanical hindrance, myocardial damage occurred, not only from advancing arteriosclerosis, but from repeated tonsillar infections.

From a study of the case described I have independently come to the same conclusion about the incision that Dr. Beck expounds; should my patient come to operation, I should approach the area on the right of the sternum. I cannot agree with the view that the Duval-Barasty incision is without profound effect on the circulation. I used this incision in a case with a diagnosis of pericardial adhesions. The patient died about twelve hours after operation with exactly the same symptoms that Dr. Elliot Cutler described in his cases of mitral stenosis. This patient had no pericardial adhesions, and nothing but exploration was attempted. Autopsy showed marked stenosis of the mitral valve.

To repeat the warning of Schmieden, left-sided adhesions should be freed first, so that the area of passive congestion is not transferred from the peripheral venous system to the pulmonary bed by release of the right side of the heart first.

DR. JOHN ALEXANDER, Ann Arbor, Mich.: Within the past year I have operated on two patients with pronounced pectis excavatum because of disabling symptoms. In the first case the sternum had gradually sunken during four years following a slight injury, which was probably not a fracture. On admission there

were dyspnea and much pain, and the heart had been forced into the left hemithorax. At an open operation I lifted the depressed sternum and its attached depressed cartilages and held them in the normal position until bony union had taken place. Nearly a year later, the boy was well and free from the symptoms that required operation.

The second patient was a young woman whose deformity followed a sternal fracture two years before operation. She had severe cardiocirculatory disturbances with disabling anginoid pains, which disappeared after operation. Operation consisted in removal of the sternum and portions of its attached cartilages and sewing the pectoral muscles together over the defect. There was direct evidence at operation of firm pressure of the sternum on the heart. In each of these cases the symptoms were probably caused by pressure on the heart rather than by pericardial adhesions.

Dr. D. B. Cole, Richmond, Va.: I rather hesitate to discuss such a brilliant presentation, but wish to report the case of a patient operated on by Dr. Frank S. Johns, who presented symptoms of pressure that were due to pericardial adhesions.

The apex beat of the heart had been pulled to the second interspace anterior axillary line, and the entire heart was rotated upward, backward and to the left. There was also an adhesion from the pericardium to the diaphragm.

The patient first developed signs and symptoms of mitral stenosis followed by those of pulmonic stenosis. His lips became cyanosed, and cardiac decompensation developed. A phrenicectomy was done with considerable relief from symptoms, especially those of decompensation. The patient continued to have signs and symptoms of pulmonic stenosis until large sections of the third, fourth and fifth ribs were removed. This gave the patient an elastic chest wall, and prompt symptomatic relief resulted. The patient has been followed up rather closely and now shows neither signs nor symptoms of cardiac disease.

Dr. Claude S. Beck, Cleveland: We feel that there should be few mistakes in the diagnosis of the Pick syndrome when it is not complicated by other cardiac abnormalities. It stands out as a fairly distinct entity. The polyserositis, with little or no subcutaneous edema, the increased venous pressure, the absence of disease of the cardiac valves and the limitation of movement of the heart during diastole and systole, when occurring together, give a fairly certain diagnosis. The cases of pericardial adhesions that are complicated by other cardiac disorders, however, are difficult to diagnose. Not only is the diagnosis of this group of cases baffling, but the result following operation for relief from the adhesions cannot be as good as in the former group.

I saw a case in consultation with Dr. Emmett Holt in Baltimore a few weeks ago in which the child evidently had adhesive pericarditis and also defective aortic and mitral valves. There was great decompensation. The heart was very much enlarged. We felt that even though the adherent pericardium were removed, the resulting condition would not be sufficiently improved to warrant operation in this case.

Concerning the degree of shock associated with the Duval-Barasty exposure of the heart, I can say that in one case in which this exposure was used—the case of a patient with a wound of the heart operated on by Dr. Harvey of New Haven—the operation did not seem to produce shock, but certainly in cases of great decompensation it has been our experience that this exposure causes a certain amount of shock.

ANTEROLATERAL COSTECTOMY FOR INADEQUATE COLLAPSE FOLLOWING POSTERIOR EXTRAPLEURAL THORACOPLASTY

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Rest, collapse and compression of the diseased lung are accepted fundamental principles in the treatment for pulmonary tuberculosis. That degree of suspended activity or compression is indicated that is necessary to bring about permanent arrest of the tuberculous lesion, to relax the tension of the scar tissue and to heal cavities. The decreased demands on respiratory function incident to physical inactivity or rest in bed may fulfil the indications. The degree of rest and partial collapse of the lung that results from paralyzing the diaphragm by phrenic crushing or evulsion may turn the tide. The effectiveness of collapse following artificial pneumothorax is due to the relatively complete collapse of the diseased lung. The failures of this method are due chiefly to adhesions preventing complete collapse, to too early abandonment of the method and to complications attributable to it.

The principles underlying posterior extrapleural thoracoplasty are practically identical with those of artificial pneumothorax. The degree of collapse of the lung resulting from it depends on the extent of that of the thoracic wall. It varies within wide limits, but is never as complete as that which follows complete pneumothorax. The results of posterior extrapleural thoracoplasty in properly selected cases are favorable in proportion as the degree of collapse fulfils the indications set by the pathologic anatomy of the lesion. A partial thoracoplasty may be sufficient in case of a strictly localized pathologic process, especially one of the apex of the lung. A limited degree of collapse of the whole thoracic wall may be equally effective in case of a more diffuse involvement, but, generally speaking, the more complete the collapse the more certain it is that the results will be favorable. Sauerbruch writes that an extensive extrapleural thoracoplasty furnishes the best mechanical and anatomic basis for the healing of the tuberculous lesion.

In any individual case the compression of the lung may be said to be adequate, even though partial or submaximal, if the indications for it are fulfilled, but this is difficult to determine beforehand. The failures of thoracoplasty to arrest the tuberculous lesion in properly selected cases are due in large measure to an inadequate degree of pulmonary compression.

The causes of an inadequate collapse following posterior extrapleural thoracoplasty may be inherent in the pathologic process or in the operative procedure.

Inflammatory thickening and deformity of the ribs and thickening of the pleura lessens the degree of collapse. A pulmonary cavity surrounded by thick walls of inflammatory tissue, especially if situated centrally, may remain incompletely collapsed. A large chronic tuberculous empyema cavity usually persists in part and always does so if there is open drainage.

The typical posterior extrapleural thoracoplasty consists essentially of resection of the upper eleven ribs flush with their respective transverse processes, in two or three stages, at intervals of from one to several weeks. Variations in this operative procedure that most influence the degree of resulting collapse are the length of segments of ribs resected and the time interval between stages.

The longer the segments of ribs removed, under similar conditions, the more complete the mobilization of the thoracic wall and the ultimate pulmonary compression. There is, however, a distinct limit to the degree of mobilization of that thoracic wall that may be induced at any one sitting without the production of paradoxic respiratory movement of the thoracic wall and mediastinal flutter. A similar mediastinal flutter may result from resecting at one stage shorter segments of a larger number of ribs. Generally speaking, the tendency to mediastinal flutter in any given case with a mobile mediastinum is proportional to the area of thoracic wall deprived at any time of its rib support.

Extensive paradoxic movement of the thoracic wall and wide amplitude of mediastinal flutter must be avoided at any cost. This was clearly demonstrated by the pioneer work of Brauer and Freidrich, who lost nearly 30 per cent of their first twenty-seven patients following complete resection of all the ribs in one stage. Any degree of mediastinal flutter always adds to the respiratory load on the other lung and therefore increases the risk of inciting to activity a dormant lesion in it. The only way to avoid it is at a sacrifice of the length or of the number of ribs resected at one stage. The beginning of paradoxic movement of the thoracic wall during the progress of the operation is ample warning.

Perhaps the most frequent cause of an imperfect collapse referable to the operation is regeneration of the ribs between stages. As is well recognized, the major amount of collapse is due to a drop of the whole thoracic wall in the long axis of the body after the thoracoplasty is completed. The longer the interval between the first and last stage, the more extensive and advanced the regeneration of the ribs, and the less the ultimate drop of the thoracic wall. But prolongation of the interval between stages may be unavoidable. Frank purulent infection

of the wound, pneumonia or activity of a tuberculous lesion in the opposite lung, severe hemoptysis or the poor general condition of the patient may necessitate a prolonged interval between stages.

A multiple-stage thoracoplasty at prolonged intervals extends the hope of a cure from pulmonary compression to a large group of patients in too poor condition to survive a two-stage or even a three-stage operation, but the resulting compression of the lung from posterior thoracoplasty alone is almost certain to be inadequate because of regeneration of the ribs. The larger the proportion of such otherwise hopeless patients the surgeon accepts for a multiple-stage operation, the greater will be his proportion of cases of inadequate collapse following posterior thoracoplasty.

The principle of complete costectomy was embodied in the single-stage operation of Freidrich and Brauer already cited. The operation, variously modified, has been described by Brunner, Welles, Jacobaeus and Kay and others, but the secondary complete anterolateral costectomy through a midaxillary incision has not received the attention it merits.

INDICATIONS

The indications for an anterolateral costectomy, as already suggested, are in part symptomatic and in part anatomic. Persistent symptoms, such as cough with bacilli-laden sputum, hemoptysis and fever, or recurrence of such symptoms, following an average degree of collapse, are indications for complete costectomy, provided causative lesions elsewhere can be excluded (fig. 1). Anatomic indications are persistent pulmonary or pleural cavities. Partial pneumothorax cavities, in my experience, are usually obliterated by an average degree of collapse of the thoracic wall combined with aspiration of the air, but when for any reason this collapse is less extensive a cavity may persist. A chronic empyema usually persists in part even following resection of very long segments of ribs (fig. 2). Such a persistent empyema may become secondarily infected or it may perforate into a bronchus, as in one of my patients, drowning him in his own pus. Prolonged absorption may lead to amyloid degeneration and other visceral damage.

Unobliterated pulmonary cavities are usually the source of persistent cough and bacilli-laden sputum and are a potential source of hemoptysis. Such cavities, if centrally situated, require the most complete compression for their obliteration.

A persistent dextrocardia may be in part corrected by the maximal collapse that results from anterolateral costectomy. In one case in my experience, a marked grade of tachycardia was promptly relieved even though the malposition of the heart was corrected only in part.

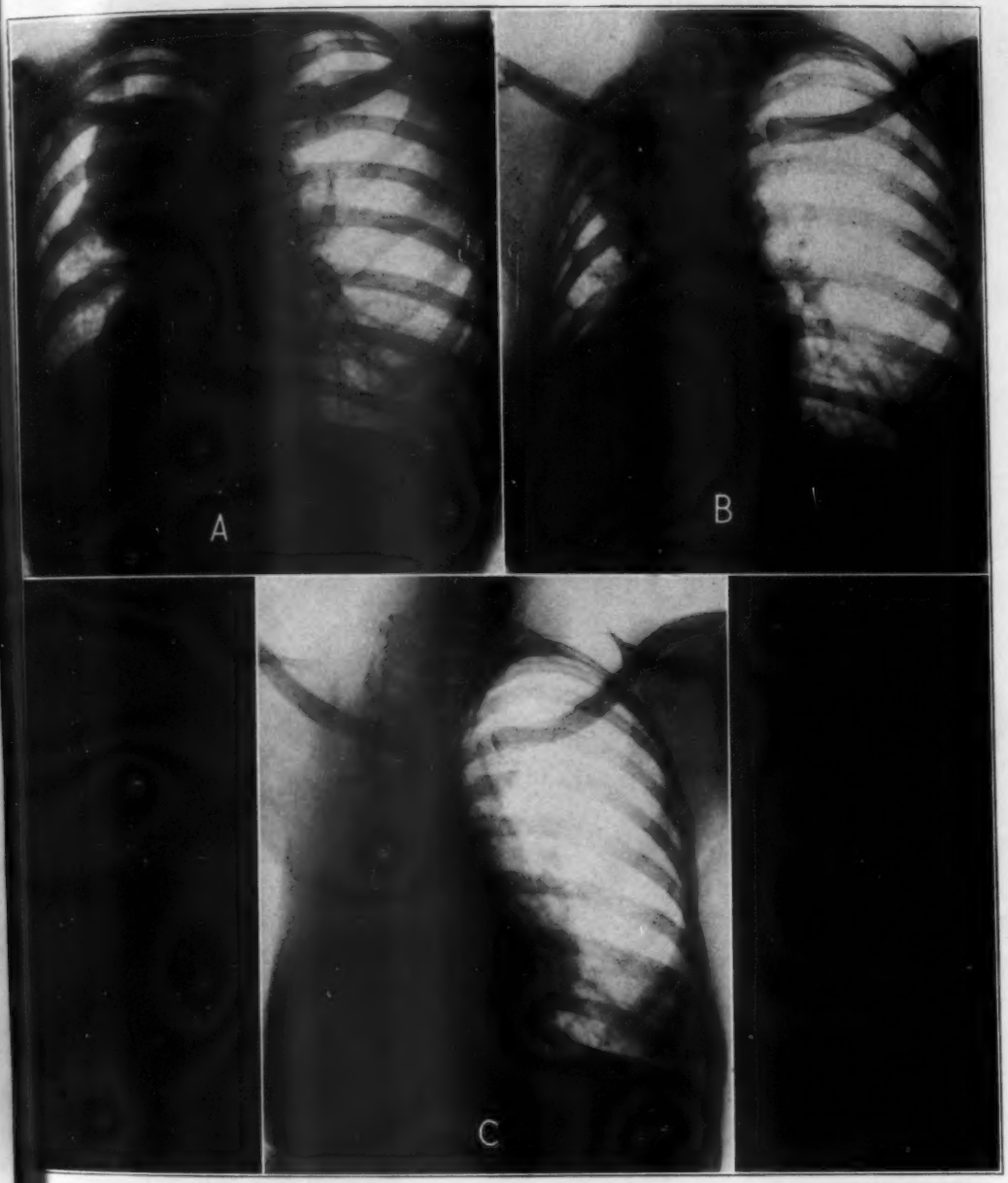

Fig. 1.—*A*, roentgenogram of a woman, aged 26. She had a fever, cough with bacilli-laden sputum, recurrent profuse hemoptysis requiring repeated transfusion of blood, which persisted after incomplete positive pressure pneumothorax collapse. Vomiting, tachycardia and prostration characteristic of profound toxemia occurred. *B*, following a three stage posterior extrapleural thoracoplasty at seven day intervals. The hemoptysis ceased, fever subsided and tuberculosis bacilli disappeared from the sputum. There was a marked gain in weight and strength during a period of five months. Following a "cold" the symptoms recurred and sputum became positive. *C*, after a two stage anterolateral costectomy at a fourteen day interval. The patient again became relatively symptom-free and has remained so during the year that has elapsed since the last operation.

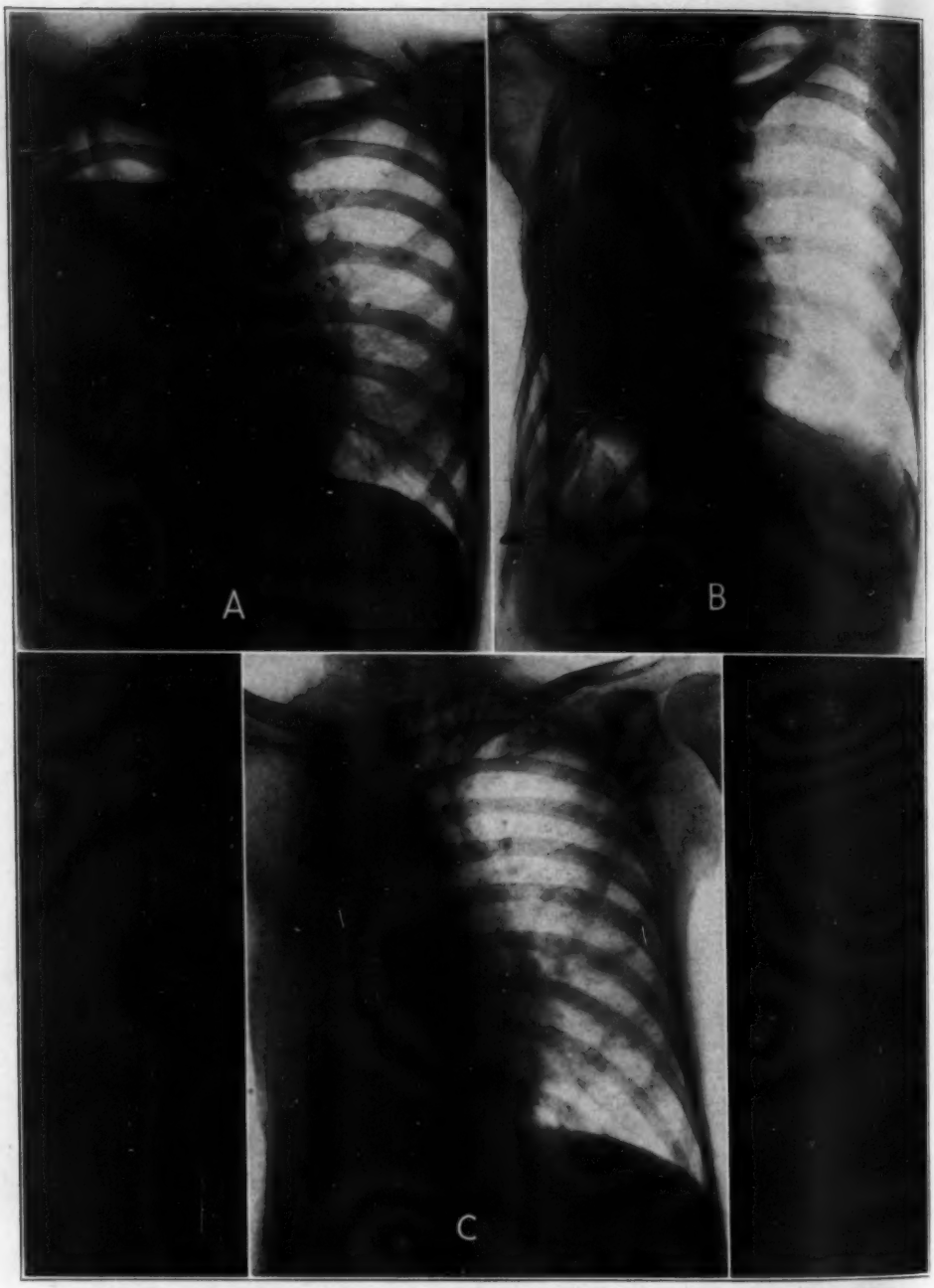

Fig. 2.—*A*, roentgenogram of a woman, aged 30, who had secondarily infected tuberculous empyema developing two months after artificial pneumothorax therapy was begun. *B*, after posterior extrapleural thoracoplasty. The residual cavity is shown filled with a sodium bromide solution. *C*, showing cavity completely obliterated following a two stage anterolateral costectomy. Residual sinus shown in roentgenogram is closed completely. Marked general improvement has persisted during the year and a half elapsing since operation.

TECHNIC

Anterolateral costectomy is technically not difficult. If the nerve trunk was crushed at the time of the posterior resection, costectomy can be done with a minimum of local anesthesia. A little gas anesthesia may be indicated only to relieve psychic stress. The incision is made in the midaxillary line (fig. 3). The muscles of the anterior and posterior axillary folds are undermined and thus not damaged (fig. 4). Usually it is desirable to remove the upper nine or ten anterolateral segments. This can be safely accomplished in two stages, the upper five being resected first. For the approach to the first rib, the position of the

Fig. 3.—Showing midaxillary incision for anterolateral costectomy.

patient is important. He lies on his side with the arm on the side to be operated on, extended above his head, where it is tied to a support. The incision extends in the axilla to the second rib. The soft tissues are next undermined, exposing the ribs.

The secret of the relative ease with which the ribs may be resected in spite of a limited exposure lies in the fact that their posterior ends are already partly mobilized and serve as a pivot on which the rib may be rotated in separating the periosteum. The rib is first liberated from the periosteum in its median, most accessible portion (fig. 5). It is then retracted outward, which facilitates separating the periosteum to the costochondral junction where it is cut. The mobilized anterior extremity of the rib can then be pulled forward, which facilitates the separation

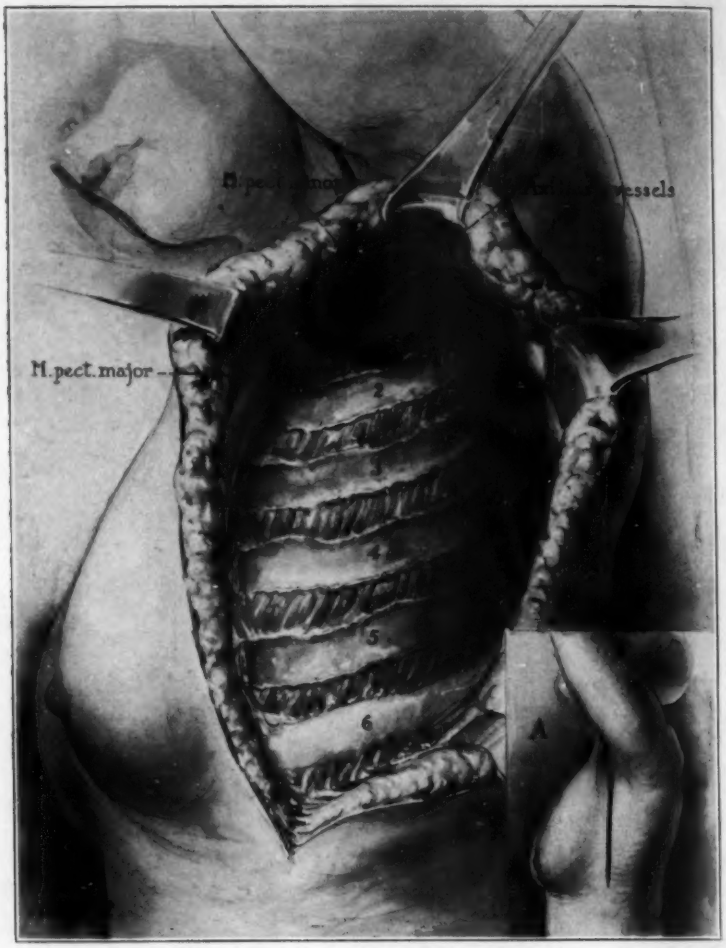

Fig. 4.—Exposure for resecting the anterolateral segments following posterior extrapleural thoracoplasty. Note good access to first rib.

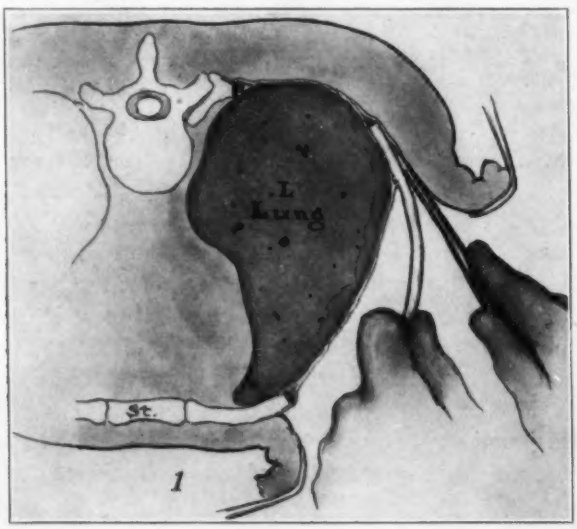

Fig. 5.—Technic for separating the periosteum from the portion of the ribs lying under the muscles posteriorly and under the scapula.

of the periosteum posteriorly. This is done first on its outer aspect, then from its upper edge. The rib is now lifted for the stripping of the periosteum from its lower edge and inner aspect. This technic reduces trauma to the intercostal vessels and consequent bleeding to a minimum. Rotation in a large arc now serves to liberate the posterior extremity. If sufficient time has elapsed between the posterior and the anterolateral resection, a spur often forms at the proximal end of the anterolateral

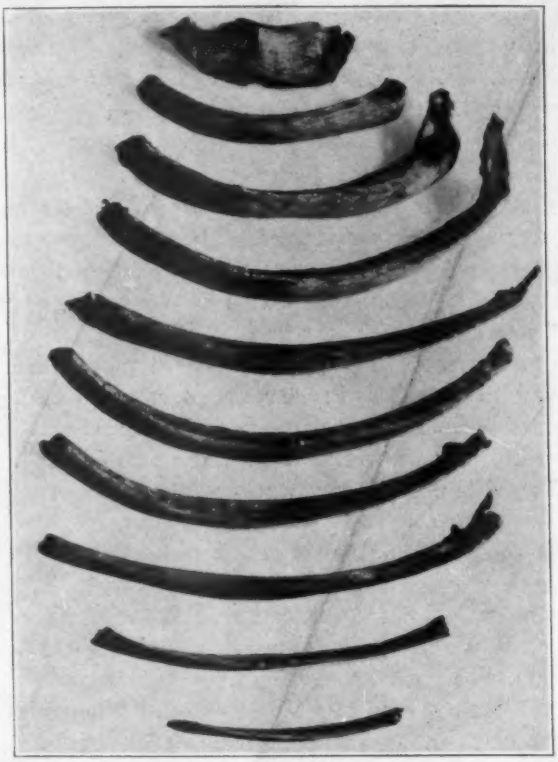

Fig. 6.—Anterolateral segments of upper ten ribs to costochondral junction; total length 157 cm. Note hooklike projection of the proximal end of third and fourth ribs.

segment to be resected. Owing to the drop in the rib following the first resection, this spur always points upward (fig. 6). When the rib is rotated on its long axis for the purpose of liberating this portion, it should be in the direction that lifts this angling spur away from the pleura. If rotated in the opposite direction, it may penetrate the lung and cause infection of the wound and a bronchial fistula. This occurred in one of my cases. Only rarely, in my experience, is union to the regenerated posterior segment so firm as to require resection. If necessary,

this can be accomplished under the guidance of the finger with an angled rib-resecting instrument.

Especial care is necessary in liberating the first rib, but if precaution is taken to keep inside the periosteal sheath, the overlying subclavian vessels will not be injured.

The fascia and skin are closed in layers with a buried Penrose drain, from which a strand of catgut extends through the lower edge of the incision. This drain is removed in twenty-four hours.

At the second stage, the incision is prolonged downward to the eleventh interspace. The lower ribs can be satisfactorily exposed through this incision. The technic for their removal is identical with that for resecting the upper ribs.

RESULTS

During the last four years I have performed this secondary anterolateral costectomy in twenty-six cases. The indications were persistent symptoms after the posterior thoracoplasty in eight cases, recurrence of symptoms after a symptom-free period of four months in one, and of ten months in another. There was an average grade of collapse of the thoracic wall from the posterior resection in all these cases. In three, regeneration of the ribs in the course of a multiple-stage operation prevented a satisfactory anatomic degree of collapse, and in all, symptoms persisted. In two, there were large unobliterated pulmonary cavities and persistent pneumothorax cavities. In eleven, there were unobliterated empyema cavities secondary to active pulmonary tuberculosis. The parietal pleura overlying a residual cavity was resected later in all of these cases, with complete healing.

In all these cases the anterolateral resection was as well or better tolerated than the posterior resection. There was one death attributable to the operation. This patient showed no more immediate reaction than the average. He ate his supper the evening of the day of operation. Gradually symptoms of an acute infection developed, and he died on the ninth day. Blood culture showed a hemolytic streptococcus. One patient had a persistent hemoptysis for which a secondary pneumolysis was performed, using the pectoral muscles to compress further the upper lobe of the lung. The hemorrhages were almost completely checked for a period of twenty-four months, but she died thirty-six months after the anterolateral costectomy, from a profuse hemorrhage. A bronchoscopic examination had been attempted on this patient at the Chevalier Jackson Clinic previous to the operation, but failed because of the profuse bleeding. One patient had a persistent mild grade of paradoxic movement of the thoracic wall, with moderate dyspnea on exertion. The lower five ribs had been resected elsewhere about a year before. The regenerated segments were removed at the posterior

operation and did not regenerate a second time, leaving the lower part of the thoracic wall permanently mobilized. In all the other cases regeneration of the ribs has occurred.

The sputum of all of these patients remained free from tuberculosis bacilli. One patient had symptoms of a mild involvement of the other lung during the first year following the operation, but these symptoms subsided. The empyema cavity in all cases is healed. Sixteen of the twenty-six patients are symptom-free, except for more or less dyspnea on exertion. One of these patients is doing heavy farm work. Eight may be classified as greatly improved, the persistent symptoms being varying grades of weakness, dyspnea on exertion and tachycardia. One has a persistent and one, recurrent attacks of unproductive cough.

There is no loss of function of arm and shoulder except some limitation in extension of the arm, in a few cases, due to the contracting scar. There is no more noticeable deformity when the patient is dressed than results from the posterior thoracoplasty. The degree of collapse of the thoracic wall and pulmonary compression is maximal in all cases.

SUMMARY

Pulmonary collapse or compression offers the best if not the only hope of a cure to patients with pulmonary tuberculosis who do not get well under modern sanatorium treatment or its equivalent.

The effectiveness of artificial pneumothorax is due chiefly to the resulting relatively complete collapse of the lung.

Posterior extrapleural thoracoplasty is identical in principle with pneumothorax.

The degree of pulmonary compression following posterior extrapleural thoracoplasty varies within wide limits, but is never as great as following complete pneumothorax. A large proportion of incomplete cures and recurrences are due to a degree of compression inadequate to the individual case.

Compression following posterior extrapleural thoracoplasty may be considered inadequate if symptoms referable to the partially collapsed lung persist or recur, or if there remain unobliterated pleural or pulmonary cavities.

The cause of an inadequate collapse may be inflammatory stiffening of the lung or thoracic wall, or regeneration of the ribs between the stages of the operation.

Anterolateral costectomy following posterior thoracoplasty consists in the subperiosteal resection of the remaining rib segments.

The indications for anterolateral costectomy are persistent or recurrent symptoms referable to the incompletely collapsed lung or to the unobliterated pulmonary or pleural cavities.

This operation results in a maximal pulmonary compression and obliterates pulmonary and pleural cavities or reduces them to a minimum size. It also facilitates pneumolysis when indicated for a persistent pulmonary cavity and is a necessary preliminary to resection of the pleura over residual empyema cavities.

The operation is technically not difficult, is relatively well tolerated and the postoperative discomfort is minimal.

By making possible an adequate degree of collapse in multiple stages at relatively long intervals, it extends the indication for pulmonary compression to a considerable group of patients in too poor condition for a two-stage or three-stage operation.

Anterolateral costectomy is the logical procedure for "following through" in cases in which for any reason compression following posterior thoracoplasty is inadequate.

In my series of twenty-six cases of anterolateral costectomy, there has been one operative death from sepsis and one subsequent death from hemorrhage. A maximal degree of pulmonary compression and obliteration of cavities was effected in all cases.

THE UNFAVORABLE RESULTS OF PHRENICECTOMY*

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During the past decade, a rather extensive literature has accumulated on the surgery of the phrenic nerve as applied to pulmonary tuberculosis, bronchiectasis and abscess of the lungs. This literature has become increasingly voluminous, particularly in the last four or five years. Most of the authors have dealt with the subject: (1) purely from the academic standpoint, (2) by reporting series of cases varying in number from 1 to 600, or (3) by combining both of the foregoing methods of approach. The technic of phrenicectomy and exaresis has been adequately described many times, and as a result the procedure, with minor individual variations, has become standardized. The accidents to be avoided and cautions against them have almost all been directed toward errors in technic and how to avoid them, and also to the possibility of grave and unavoidable mediastinal hemorrhage.

Among the technical errors that have occurred, even with experienced operators, are injury to the thoracic duct, the vagus or the sympathetic nerves, the brachial plexus, the adjacent great vessels or important branches of them and the dome of the pleura. These and the anomalies or abnormal positions of the phrenic nerve itself have already been detailed at length so often and so well that I need waste no time on them. Furthermore, they should always be to the fore in the mind of any surgeon while performing operations in this region.

I shall not discuss the indications for phrenicectomy: whether the nerve should be crushed, divided, resected or avulsed; nor the results obtained from these various procedures. I have attempted no analysis of my 160 cases quoted herein, which comprise operations of all the aforementioned types by Drs. Lambert, Greenough, Weeks and myself in various institutions during the past five years. This study has been strictly limited to a small group of cases in which there have been unfavorable reactions immediately following operation on the phrenic nerve that has resulted in paralysis of that portion of the diaphragm supplied by it. In all of these instances the operative procedure has been perfectly performed without technical slip of any sort. Except for the possibility of mediastinal hemorrhage, this phase of the subject has scarcely been mentioned in the literature of any of the English speaking

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countries, doubtless for the reason that the chances for poor results directly attributable to the operation have been considered to be negligible. The operation is usually presented to the patient as one without risk, which the surgeon hopes will prove of great benefit, but which in all events can do no harm. That accidents and complications can and do occur, however, in no way referable to the operative technic, has been recognized especially by the Germans, and numerous cases of such sequelae have been reported by them; a few have also been reported by the French and Italians. In some of these the outcome was fatal; in some the patients recovered.

From a review of the literature of the past five years I have obtained a total of 4,697 cases of phrenicectomy, including crushing and simple division of the nerve. Of these, 3,050 were reported by Germans and Austrians, 1,217 by Americans, English and Canadians, including my series, and 430 by French and Italians. The individual series recorded by these authors consisted of from 1 to more than 600 cases. In this entire group of 4,697 cases there have been 57 (1.2 per cent) complications directly attributable to the operation, and of these, 26 (0.5 per cent) were fatal. It thus becomes clear that when these sequelae occur they are of a most serious nature, as over 40 per cent of them have ended in death.

HEMORRHAGE

As the phrenic nerve and its accessories, in part of their course, lie in intimate contact with the subclavian, jugular and innominate veins, and the subclavian, internal mammary and pericardiophrenic arteries, hemorrhages that occur are ascribed to trauma to one of these vessels by the avulsion of the nerve. Most commonly they seem to be due to a tear of the pericardiophrenic artery, although injuries to the large veins have also been mentioned. Two instances of fatal hemorrhage have been reported by Kleinschmidt [1] as having occurred in Sauerbruch's clinic, another by Rist, one by Thomopoulos [2] and two by Herben,[3] six in all. Likewise, Matson [4] mentioned a case of nonfatal hemorrhage due to pulling away a bit of the wall of the jugular vein. It is easy to understand how this danger would probably be greatest with those patients in whom fibrous mediastinitis is present with marked scarring and retraction. Fortunately, I have not as yet met with this terrifying catastrophe. Furthermore, whenever the nerve cannot be readily drawn up from the mediastinum or when a chronic mediastinitis is recognized or suspected,

1. Kleinschmidt, P.: Deutsche med. Wchnschr. **53**:473, 1927.
2. Thomopoulos, A.: Paris, 1925.
3. Herben, G. F.: Personal communication to the author.
4. Matson, R. C.: Tr. Coll. Physicians **49**:167, 1927.

I am always satisfied with a moderate resection of the nerve such as may be obtained without undue traction.

Matson, in his excellent article, described the presence of a small bit of anthracotic lymph gland that accompanied an avulsed nerve in one instance, and mentioned this as an etiology for a possible suppurative mediastinitis. No such cases have been reported up to the present, however. Of a somewhat similar nature, but due to a tear of the mediastinal walls, are two cases reported by Deist [5] and another by Sergent, Baumgartner and Bordet.[6] In Deist's patient a pneumothorax developed, and later a pyopneumothorax, following avulsion of the nerve; in Sergent's case, exaresis of the nerve caused pneumothorax and mediastinal emphysema. Both of these patients died.

Other causes of death have been given as follows: Berg [7] described death six hours after operation from pulmonary embolism as shown at autopsy. Chandler [8] ascribed death in his patient four hours after operation to pulmonary edema. Curti's [9] patient died in ten days with persistent dyspnea and tachycardia. Hedblom [10] reported one death from respiratory insufficiency. Leriche's patient with bronchiectasis, mentioned by Sergent and his collaborators, died on the operating table of asphyxia shortly after the nerve had been avulsed. Necropsy showed the opposite lung flooded with the secretions; hence the patient, dyspneic and with his ability to cough diminished, had literally drowned in his own secretions. The remaining thirteen deaths in this group of fatalities, including the case to be cited, were due to pneumonia or a spread of the tuberculous process in either or both lungs immediately subsequent to operation (table).

Thirty-one patients, although they survived, were made distinctly worse by the operative procedure, which seemed to produce either a prompt spread of the disease or the development of pneumonia in one or both lungs. There is one exception, the case of a patient with tuberculosis and positive sputum, reported by Loewenthal.[11] Following phrenicectomy, a typical abscess with cavity formation, fluid level and characteristic abscess sputum appeared in the lung of the side on which operation had been performed and then gradually cleared up spontaneously.

5. Deist, H.: Beitr. z. Klin. d. Tuberk. **63**:424, 1926.

6. Sergent, E.; Baumgartner, R., and Bordet, F.: Bull. et mém. Soc. méd. d. hôp. de Paris **50**:20, 1926.

7. Berg, W.: Deutsche med. Wchnschr. **54**:874, 1928.

8. Chandler, F. G.: Brit. M. J. **2**:605, 1928.

9. Curti, E.: Policlinico (sez. prat.) **34**:1474, 1927.

10. Hedblom, C. A.: J. Michigan M. Soc. **28**:535, 1929.

11. Loewenthal, M.: Beitr. z. Klin. d. Tuberk. **71**:712, 1929.

REPORT OF CASES

CASE 1.—M. K., a woman, aged 35, single, was admitted to Summit Park Sanatorium in December, 1926. There was extensive tuberculosis of the right lung with fibrosis and cavitation and with considerable retraction of the heart and trachea to the right. The left lung contained a healed lesion at the apex. Sputum was positive. She improved very slowly while at the sanatorium, and it was finally thought that phrenicectomy might be beneficial. This was performed on Nov. 21, 1928, and was followed by considerable gastric disturbance. Fluoroscopic

Causes of Death Following Phrenicectomy

Author	No. of Cases	Cause of Death	Time
Berg, W.: Deutsche med. Wchnschr. **54**: 874, 1928	1	Pulmonary embolism	6 hours
Chandler, F. G.: Brit. M. J. **2**: 605, 1928.....	1	Pulmonary edema	4 hours
Curti, E.: Policlinico (sez. prat.) **34**: 1474, 1927	1	Dyspnea and tachycardia...	10 days
Dumarest and Berard: Rev. de la tuberc. **9**: 161, 1928	2	Contralateral spread of tuberculosis	?
Deist, H.: Beitr. z. Klin. d. Tuberk. **63**: 424, 1926	2	Pneumonia; pyopneumothorax	?
Hedblom, C. A.: J. Michigan M. Soc. **28**: 535, 1929	1	Respiratory insufficiency....	?
Kleinschmidt, P.: Deutsche med. Wchnschr. **53**: 473, 1925	2	Hemorrhage caused by avulsion of nerve	?
Morone, G.: Ann. ital. di chir. **4**: 189, 1925.....	1	Pneumonia	9 days
Schnippenkotter, W.: Beitr. z. Klin. d. Tuberk. **65**: 56, 1927	1	Spread of tuberculosis.....	?
Schurch, A.: Beitr. z. Klin. d. Tuberk. **61**: 552, 1925	1	Contralateral spread of tuberculosis	?
Sergent, E.; Baumgartner, R., and Bordet, F.: Bull. et mém. Soc. méd. d. hôp. de Paris **50**: 20, 1926	3	Spontaneous pneumothorax and mediastinal emphysema; on table of asphyxia; hemorrhage, 24 hours	1 day
Zodek	5	Pneumonia or spread of tuberculosis	?
Herben, G. L.: Personal communication to the author	2	Mediastinal hemorrhage ...	?
Miller, J. A.: Personal communication to the author	1	Pneumonia	Several weeks
Thomopoulos, A.: Paris, 1925.....	1	Hemorrhage from pericardiophrenic artery	?
Berry	1	Pneumonia and edema.....	24 hours
Total.....	26		

examination three days later revealed the heart pulled even more to the right than formerly and the trachea markedly deviated to that side. The diaphragm could not be seen, because a dense shadow obscured the diaphragm and lung on the right, except for the cavity in the upper lobe, which now appeared more sharply defined than previously.

On physical examination, there was marked dulness over the right side of the chest, but the breath sounds were clearly heard. X-ray films merely confirmed the fluoroscopic observations. Symptomatically, the patient was perfectly comfortable. She did not do well, however, and in August, 1929, had a profuse hemoptysis, after which the signs of a large antrum in the lower lobe of the right lung appeared. In December, 1929, roentgenograms still showed a massive atelectasis on the right and now some fresh infiltration in the left upper lobe. Bronchoscopic examination showed a marked angulation of the right main bronchus, and the mucosa of the bronchus of the middle lobe was swollen and

bled easily. This obscured the picture, but it was thought that there was in addition a definite obstruction in the bronchus of the lower lobe. At present the patient is at home and gradually going downhill.

It would appear that phrenicectomy in this case, for some unexplained reason, caused a massive atelectasis of the homolateral lung which was accompanied by almost no symptoms, but which, nevertheless, has resulted in a steady progression of the disease. It was advocated here as a test operation before and as an aid to thoracoplasty, but the outcome was poor.

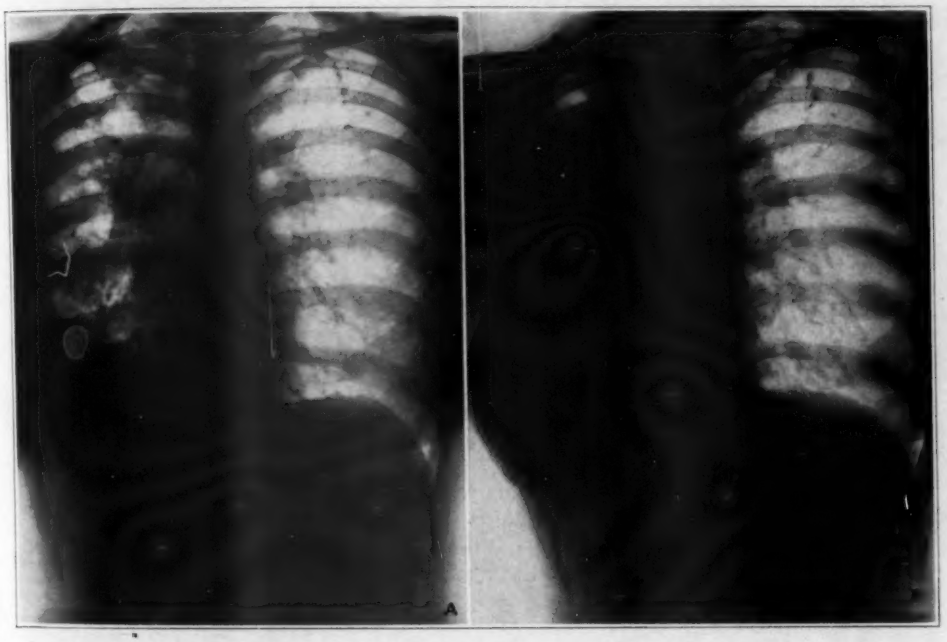

Fig. 1 (case 1).—*A*, before phrenicectomy. *B*, after phrenicectomy. Massive atelectasis is present.

CASE 2.—M. I., a woman, aged 30, had a history of "bronchitis" for several years with two hemoptyses, one in 1922 and the second in 1928. She had taken rest treatment intermittently, and for nine months previous to her admission to the Fifth Avenue Hospital, in January, 1929, had noticed some pain in the lumbar region. Roentgenograms of the lungs and back revealed an extensive fibrocaseous tuberculosis of the right lung with cavities in the upper lobe and considerable fibrosis in the lower lobe. On the left side there was early infiltration in the upper lobe and some thickening about the hilus. Also, there was partial destruction of the third and fourth lumbar vertebrae and the intervertebral disk. At that time the patient was raising about 120 cc. of sputum a day. She was in bed on a Bradford frame from Jan. 17 to June 5, 1929. From May 24 to June 5, she had daily hemoptyses varying in amount from 50 to 500 cc., and on June 1, was given a transfusion of 300 cc. of blood. Right phrenicectomy was performed on June 5

with the hope that the bleeding might be arrested. At that time the temperature averaged from 99 to 100 F.; the pulse rate was from 90 to 120, and respiration, 26. Immediately following operation there was dyspnea with a pulse of from 120 to 140 and a respiratory rate of 32 and later 40. There was a rise in temperature to 101 F., and twenty-four hours later a drop to 97 F. Cough and sputum diminished markedly at once. Her physical signs, however, were those of steadily increasing moisture throughout both lungs, and medium and coarse râles could be heard everywhere. The dyspnea and râles increased, she became cyanotic, and finally died forty-five hours after operation.

In this instance phrenicectomy was advised almost as a last measure. The disease had already lighted up and was progressing rapidly with daily large hemoptyses. It was hoped that phrenicectomy might control these. Instead, her already delicate cardiorespiratory balance was upset and her ability to cough hindered, with resultant prompt bronchiogenic spread and death.

Case 3.—C. B., a man, aged 35, had had tuberculosis for five years. The lesion was extremely fibroid and was confined entirely to the right lung, chiefly the upper lobe. There were two small cavities at the apex and tremendous fibrosis with marked retraction of the heart to the right, pulling up of the right side of the diaphragm and pronounced displacement and angulation of the trachea. In fact, the pull on the trachea was so marked that the patient became dyspneic on relatively slight exertion. In addition, exercise produced occasional small hemoptyses. The temperature varied between 98 and 99 F.; the pulse rate was 90, and the respiratory rate, 18. Phrenicectomy was performed on March 6, 1930. The dyspnea increased immediately, and the hemoptyses continued. The temperature rose to 101 F. for forty-eight hours; the pulse rate was 100 and the respiratory rate from 26 to 30 for five days. Roentgenograms showed diffuse shadows all over the right pulmonic field, the trachea even more deviated to the right than formerly and the heart entirely within the right side of the chest. The symptoms gradually cleared up, so that there was eventually less dyspnea than before operation, and x-ray films showed a disappearance of the atelectasis with a return of the heart and mediastinum to their former positions. Nine weeks after operation, the patient's condition was about the same as before the phrenicectomy.

In this case phrenicectomy was performed to lessen the dyspnea and hemoptysis. A temporary atelectasis appeared on the operated side without untoward results. So far, however, there has been no benefit.

Case 4.—M. K., a girl, aged 19, had had fibroid phthisis of the lower lobe of the left lung for two and a half years. In November, 1929, an acute lesion developed in the upper lobe of the right lung. This gradually responded to absolute rest, but late in February, 1930, a cavity appeared in the old process in the left lower lobe. She was in excellent condition, with a temperature of only 99 or 100 F. It was felt that a phrenicectomy was indicated and would be most beneficial. This was done on March 14. That evening she was somewhat dyspneic and her temperature was 102 F. The following morning her temperature was 105 F.; the pulse rate, 150, and respiration, 30. Over the left lower lobe there were marked dulness and complete absence of breath sounds and râles. A diagnosis of massive atelectasis of the left lower lobe was made, and confirmed later by a roentgenogram.

Fig. 2 (case 4).—Before phrenicectomy. There is a healing lesion on the right, with fibrosis, and a cavity in the left lower lobe.

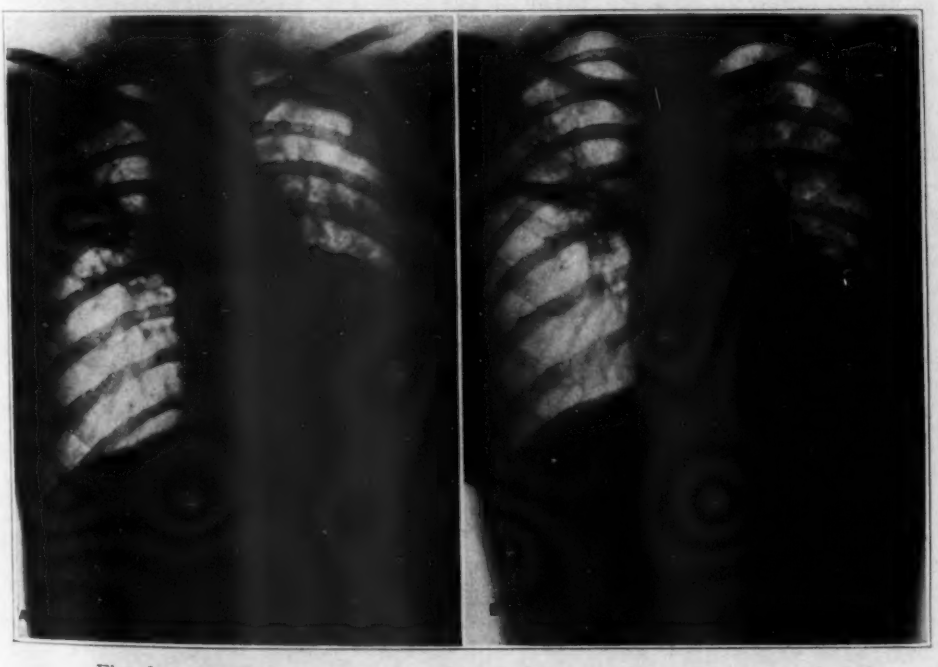

Fig. 3 (case 4).—*A*, twenty-four hours after operation. There is massive atelectasis of the left lower lobe. *B*, forty-eight hours later. The atelectasis has cleared up, with a return of the mediastinal structures to their normal positions. Bronchopneumonia.

The next day dulness was less and breath sounds and râles could be heard over the affected lobe; twenty-four hours later a second x-ray film showed an apparent bronchopneumonia of this portion of the lung. The heart had returned to its normal position, and the lung appeared well aerated. After about a week her temperature, pulse and respiratory rates came down, and she improved steadily. Bronchoscopy was not performed, because she never looked as ill as her pulse and temperature seemed to indicate, and she was always able to cooperate well and to cough freely.

In this case I felt that the collapse of the lower lobe immediately following phrenicectomy was so great, owing to the high rise of the diaphragm, that there was temporary interference with the drainage of the cavity and a resulting plugging of the bronchus of the lower lobe with thick secretions. Atelectasis developed, with a sharp general reaction. This soon cleared, however, but was followed by a mild bronchopneumonia, fortunately with rapid improvement.

SUMMARY

I have endeavored to point out that there is a definite risk associated with crushing, resection or avulsion of the phrenic nerve. Fifty-seven cases, four of which are my own, have been reviewed in which phrenicectomy was most detrimental; twenty-six of the patients died as a result of the operation. These poor results have all been subsequent to properly performed operations without technical error. In view of the fact that there is such widespread advocacy of phrenicectomy as a harmless procedure in cases of pulmonary tuberculosis, bronchiectasis and even abscess of the lungs, it would seem wise to sound a word of caution and to call attention to the risk involved, slight though it is.

CONCLUSIONS

How may these accidents be avoided? As to the selection of cases, Dumarest and Berard [12] have mentioned that there is less danger of mishap in cases that have become more or less stabilized. Patients in whom the disease is acute and progressive do not respond so well. Case 2, in which the patient died, is an example of this.

Another group of patients who may have trouble are those with large amounts of sputum, as in bronchiectasis, or an extensive fibrocaseous type of tuberculosis, in which it is essential for drainage that coughing be free and unobstructed. Phrenicectomy does not always facilitate cough and expectoration; occasionally, it works just the other way. This is well demonstrated by the case of bronchiectasis reported by Sergent, Baumgartner and Bordet; [6] again by case 2, and more recently by a patient of Dr. James A. Miller [13] with bronchiectasis. Operation so

12. Dumarest and Berard, L.: Rev. de la tuberc. **9**:161, 1928.
13. Miller, J. A.: Personal communication to the author.

hindered cough and drainage, with resultant decrease in sputum, that the secretions puddled in the lung, and an extensive fatal pneumonia developed. I therefore feel that phrenicectomy is a serious procedure in this type of case also and should not be undertaken without full realization of the possible consequences.

With the foregoing facts in mind, it may be possible to eliminate some of these unforunate complications. It is not my wish to detract in any way from the value of phrenicectomy or the great benefits derived from it in all properly selected cases. I wish merely to place before the medical profession the fact that there is a certain risk (1.2 per cent) of poor results associated with it, and a mortality of about 0.5 per cent.

Finally, is it not possible that perhaps these figures do not represent all of the unfavorable results and fatalities that have followed phrenicectomy?

MECHANICS OF COLLAPSE THERAPY AND ITS INDICATIONS

OBSERVATIONS IN SEVEN HUNDRED CASES

E. J. O'BRIEN, M.D.
DETROIT

Among thoracic surgeons and others interested in the treatment for pulmonary disease, there still seems to be a divergence of opinion as to the mechanics involved in collapse therapy. My only justification in presenting this paper, which dwells chiefly on the fundamental principles involved in these procedures, is to present my deductions on the subject, based on observations on 700 operative cases. I hope that it will bring out discussion that may lead to a better understanding.

While in a few patients with pulmonary tuberculosis the lesions heal by resolution, as do those in nontuberculous pneumonia, by far the greater number heal after the formation and contraction of newly formed, fibrous, connective tissue has caused their encapsulation. Rest to the lung, by causing a slowing of the lymph flow and a retarded circulation, results in a lessened toxemia and an increased production of this fibrous tissue. By prohibiting this rest and unfavorably influencing the closure of cavities when they exist, the normal respiratory cycle retards rather than promotes healing of these lesions, as becomes apparent when one reviews the physiology of respiration.

MECHANISM

While the mechanism involved in the respiratory cycle is complicated, the underlying principles are simple. In the normal condition, except for enough fluid to moisten their surfaces, the lungs completely fill the thoracic cage, and as a result the elastic tissue with which they are supplied must be stretched sufficiently to accomplish this. Because of this elastic tissue, the lungs are constantly tending to contract and collapse away from the thoracic wall, but there is an adhesive force between the parietal and visceral pleura which keeps these surfaces in contact.

The result of these two forces is a tension which is called negative, i. e., less than atmospheric pressure. During inspiration, the thorax is enlarged and the tendency is to pull the thoracic wall away from the lung, which act, of course, must increase this intrapleural negative tension and stretch the elastic tissue of the lung still further as more air is sucked down the trachea to fill the air spaces. The diaphragm is the chief muscle that enlarges the thorax from above downward, whereas

the enlargement in the transverse diameter is accomplished by the elevation of the ribs. The muscles chiefly involved in this are the external intercostals and the serratus posticus superior. Other accessory muscles are also used.

Expiration is mostly a passive phenomenon. When the inspiratory muscles cease to contract, the thorax sinks and is diminished in size. This allows the elastic tissue of the lung to contract and reduce its volume. This constant activity of respiratory movements greatly interferes with perfect rest for lesions in the lung. During rest in bed, the respiratory rate is reduced, and as there is no need for excessive inspiratory movements to enlarge the thorax, the resultant quiet breathing affords some rest and reduction of lung volume, which explains the efficacy of this form of treatment in pulmonary disease. Unfortunately, in a large number of patients with pulmonary tuberculosis the rest thus afforded is not sufficient to allow healing, and additional rest must be given. That collapse therapy is so rapidly coming into extensive use in the treatment for this disease is readily understood when one bears in mind that it is the only method of securing this added rest.

Artificial pneumothorax (by reducing intrapleural negative tension), operations on the phrenic nerve (by paralyzing the diaphragm) and thoracoplasty (by removing the rigid, bony support of the thoracic wall and impairing the functions of inspiratory muscles) diminish the size of the hemithorax or the space in which the lung moves, and allow still further relaxation of elastic tissue, reduction in lung volume and limited inspiratory excursion. Rest is measured in direct proportion to this limitation.

I believe that in most instances surgical procedures act in a passive way by relieving an active inspiratory menace and result merely in an exaggerated expiration. For this reason, I prefer to use the term collapse or relaxation therapy rather than compression therapy in relation to these measures. That they do act in this manner is clear because they do nothing to the lung itself but merely overcome the untoward effects of the respiratory cycle and of the structures surrounding the lung which are preventing it from contracting of its own accord.

With pneumothorax, one can cause almost complete collapse of the lung, and this is done under negative tension in most instances. Here it is obvious that there could be no compression.

During thoracoplastic operations, the lung can be seen to contract and collapse as soon as the rigid, bony wall which has been preventing it from doing so is removed. The amount of collapse allowed by this procedure is usually in direct proportion to the amount of ribs removed. That this is true is borne out by the fact that the Brauer operation, in which large lengths of rib are removed, causes more reduction in lung volume than does the Sauerbruch operation in which only small seg-

ments are removed, and also by the fact that with anterolateral thoracoplasties, in which the remaining portions of ribs are removed, still greater reduction in volume is accomplished. That actual pressure is not exerted on the lung in these patients has been proved by the readings of intrapleural pressures following thoracoplasty. These readings were found to be negative. This, then, is also relaxation.

Operations on the phrenic nerve accomplish a similar result. The diaphragm is paralyzed, loses its muscle tone and ceases its movements. It becomes thin and fascia-like, which makes it more susceptible to intra-abdominal and intrapleural pressures. This results in its being sucked up higher into the thorax by the negative tension existing there causing reduction in the size of the hemithorax from above downward, which releases the elastic tension in the lung in direct proportion to its elevation.

I believe that actual compression is exerted only when pneumothorax is carried on to a positive pressure or when direct pressure is made over a cavity wall by using muscle or some foreign substance as a packing, as is done in apicolysis and other forms of extrapleural pneumolysis. That the weight of the soft tissues overlying the lung after thoracoplasty and the intra-abdominal pressure following phrenicectomy cause some pressure is probable, but as the lung, because of its elastic tissue, recoils and contracts away from these forces, there can be no pressure unless it occurs after the lung has been fully contracted. This condition, however, rarely exists.

If a cavity exists in pulmonary tissue, there is no natural tendency for it to close, as the act of inspiration, by enlarging the thorax and stretching the elastic tissue surrounding the cavity tends to enlarge it, and these procedures which release elastic tension and allow the lung to contract assist in the cavity's closure. In principle, this closure of cavities in the lung by surgical procedures is analogous to the simple experiment of making a hole in a piece of rubber tissue. If the rubber is stretched, the hole becomes larger; if it is relaxed, the hole becomes smaller.

Whether or not cavities within the substance of the lung and surrounded by alveolar and elastic tissue will close on release of elastic tension following surgical measures, depends on several factors: first, the size of the cavity and the amount of reduction obtained in the size of the hemithorax and the volume of the lung, and second, the thickness of the cavity wall, those with thick walls being much harder to close than those with soft walls. We surgeons have seen thick-walled cavities displaced but unchanged in size even with marked contraction of the lung around them. Sometimes even actual compression fails to close them.

Cavities situated at the periphery of the lung and in which the cavity wall is in direct contact with the parietal pleura are also hard to close, as there is no elastic tissue surrounding them which can contract and help in their closure when the tension is released. These may be closed by a complete collapse of the lung by pneumothorax, which may have to be carried on to a positive pressure; or, if they are situated at the apex of the lung as is usually the case, they may be closed when phrenic operations have caused a reduction in the size of the hemithorax, and the contracted lung, in adjusting itself to the reduced space, migrates upward away from the ascending diaphragm in the line of least resistance. If these cavities are situated at the base of the lung, with the wall resting on the diaphragm, direct relaxation of their wall with possible obliteration may take place when this muscle is paralyzed.

When the cavity wall is adherent to the thoracic wall, it may be necessary to perform thoracoplasty which will remove the rigid, bony framework that tends to keep the cavities open and allow a relaxation of the cavity wall to occur. All pulmonary cavities, wherever situated, are, of course, favorably influenced by this procedure, because it causes marked diminution in the size of the hemithorax and the volume of the lung. Thick-walled cavities at the periphery of the lung are almost as difficult to close as are those situated within the substance of the lung, as their walls do not collapse readily.

INDICATIONS

Which of the many surgical procedures is to be used in any given case is often difficult to determine. In the *Journal of the American Medical Association* of Feb. 9, 1929, and in the November issue of the same year of the *American Review of Tuberculosis*,[1] I published papers in which I discussed fully the indications for each procedure from the anatomicopathologic characteristics of the lesion, and these articles may be referred to for my views on these points. After carefully analyzing my experiences and results in the large number of patients referred to in the title of this paper, I have changed my views only in extending my indications and am now employing these procedures in a wider range of patients, more especially in those with bilateral tuberculosis.

It is no longer necessary to defend these procedures, but the extent to which they should be used is still a question of debate, many physiotherapists still being conservative about them and others wishing to employ them in almost every suitable case. There can be only two reasons for not immediately instituting some form of surgical collapse for

1. O'Brien, E. J.: Surgery of Phrenic Nerve and Intrapleural Pneumolysis, J. A. M. A. **92**:463 (Feb. 9) 1929; Am. Rev. Tuberc. **20**:787, 1929.

unilateral lesions, one being that the lesion is so small that one is optimistic enough to believe it will get well on rest in bed alone; the other, that such a measure could not help. In my opinion, the latter reason would apply only to patients with a pneumonic or consolidated lung or with other complications that would make collapse of the lung seem useless.

One has so often seen rapid increase in small lesions which one hoped could be healed by ordinary rest in bed that this type of lesion is now looked on with more suspicion. It is a benign lesion indeed in the treatment of which I do not feel that at least a crushing of the phrenic nerve should be resorted to in order to give the patient the benefit of the additional rest afforded while the diaphragm is paralyzed. In my experience, even in this group of patients, the time allowed before the diaphragm resumed its function was not sufficient to cause complete healing, and the nerve usually had to be removed later.

There can be no question but that collapse therapy in some form should be used when ordinary rest in bed and other accepted methods of treatment have been tried and the lesion is not healing. As there should no longer be a question of the merit of these procedures, if they are not to be used more extensively, it must be on the ground that they are too great a risk to the patient or too great a burden on the contralateral lung.

The mortality from phrenic operations is, of course, negligible. In my experience, the mortality from thoracoplasty is about 6 per cent. In my opinion, this mortality rate in the class of patients in which these measures are indicated, argues for, rather than against, a more extensive use of collapse therapy.

A large percentage of my patients have had bilateral lesions, and my observations have been that, in a good percentage of these, the disease in the contralateral lung has healed along with that in the side on which operation was performed, showing that no so-called "added burden" had been placed on it. I have not been convinced that any of these measures have been the direct cause of spread or activation of disease in the other lung. These constantly occur in patients under routine treatment by rest in bed, and I have seen patients in whom the lesion spread to the good lung between the time it had been decided to operate and the time the operation was to have been performed. If these patients had been operated on, the operative procedure would have been blamed. I have seen lesions or so-called "spreads" occurring after operation that have cleared up promptly in spite of the surgical procedure on the opposite side that was supposed to have been their cause.

There is, as a rule, a greater tendency to contraction in the diseased area than in normal lung tissue, and I often obtain a selective collapse without much loss of alveolar function. While the normal person has a much larger amount of alveolar space than is necessary to carry on life, there is in most cases a compensatory hypertrophy of the other lung following collapse therapy. This does not mean that an added burden is thrown on the disease in that lung, but rather that more air cells are being used than previously.

In the attempt to understand more clearly just what does take place following collapse therapy, I studied a series of patients on whom phrenicectomy had been performed. Dr. Werner presented a paper at the National Tuberculosis Society at Memphis this year in which complete observations, taken at regular intervals until the vital capacity returned to normal, were recorded. It was found that following phrenicectomy there was an immediate decrease of about 32 per cent in the vital capacity in all patients. In all but one patient, the tidal air decreased. The consumption of oxygen, however, remained practically unchanged. This, of course, necessitated some compensatory mechanism. The compensation was found to take place in three different ways with practically an equal number of patients in each group. In group I, the compensation was achieved by an increase in the respiratory labor only. In group II, the compensation was achieved by a better utilization of the inspired air, with no change in the respiratory labor, and in group III, it was accomplished only by a more efficient utilization of oxygen, with a decrease in the respiratory labor. There was no evident correlation between the extent and the pathologico-anatomic type of the lesion and the mechanism of compensation following the operation. The fact, therefore, that following phrenicectomy over two thirds of the patients achieved compensation for this reduction in vital capacity without increased respiratory rate means that an added burden is not thrown on the lesion in the other lung, but that probably an increased circulation in the contralateral lung accounts for both the better utilization of oxygen and the improvement usually seen in lesions existing in this lung. It may be significant to note that in about 70 per cent of my operative cases the lesions in the contralateral lung improved. This percentage is practically that of the two groups in which better utilization of oxygen was achieved without increased respiratory labor.

That there is a compensatory hypertrophy of the contralateral lung following collapse therepy, however, is shown by Sieper,[2] in an article

2. Sieper, H.: Die Vitalkapozität bei der Lungenphthise, besonders bei der Lungencollapstherapie, Beitr. z. Klin. d. Tuberk. **65**:725, 1927.

published in 1927 in the *Beiträge zur Klinik der Tuberculose und spezifischen Tuberkulose-Forschung.* The author had a pneumothorax of the right side performed on himself. He found that the drop in vital capacity after each inflation of air was equal to the volume of air introduced into the pleural cavity, as long as the intrathoracic pressure was kept within moderate limits. After the initial drop, the vital capacity increased during collapse. The increase was definitely faster than the resorption of intrapleural air, and it reached the original level before the pneumothorax was completely resorbed. After the resorption of the pneumothorax, the vital capacity was greater than before the treatment. Sieper attributed the increase in vital capacity to the depression of the diaphragm and increase in the circumference of the thorax or, in other words, to hypertrophy. In patients with pulmonary tuberculosis, the vital capacity following the inflation of air is greater than the difference between the original vital capacity minus the inflated air. This fact is explained as follows: The pulmonary tissue surrounding tuberculous foci frequently does not participate in the aeration process. The vital capacity of such a patient is, therefore, smaller than could be expected from the size of his foci. The collapse of such areas does not decrease the vital capacity of the patient. It follows that the vital capacity after the induction of pneumothorax will be higher the more damaged tissue is collapsed in proportion to normal tissue.

It is apparent, therefore, that while under collapse therapy the diseased area does not require the utilization of compensatory mechanism, but that under any form of collapse therapy some normal lung tissue is usually collapsed which necessitates such compensation. This compensation therefore takes place, as has been explained, but it does so without throwing an added burden on the lesions existing in the contralateral lung.

As no procedure or treatment will cause all lesions to heal, these lesions sometimes continue to increase on the collapsed side; it is not surprising, therefore, that lesions in the opposite lung also become worse. However, this does not warrant the assumption that collapse therapy has had a deleterious effect on them.

It must be understood that collapse therapy in any form is not curative but merely puts the patient in the most favorable condition for healing. The use of this procedure on patients who are obviously not doing well and the following immediate improvement prove only that this therapy has a distinct value in the arrest of the disease; such results do not justify a belief that collapse therapy should be used only in this group of patients.

As inherited resistance to this disease plays an important part in the success of any treatment, the employment of surgical procedures is not as effectual in the Mexican, the Indian and the Negro as in other races, and it is more often in this type of patient that so-called "spreads" are found.

Obviously, collapse of the lung should not be instituted if the fields of both lungs are so involved with disease and the vital capacity is so low that the patient's respiratory ability might be endangered. However, even if there is considerable disease, with cavitation, in the contralateral lung, collapse therapy may be begun on the other side if it seems advisable. This is possible because of nature's generosity in providing a superabundance of alveolar space and because of the passive action of these procedures. Partial bilateral collapse may also be instituted without endangering the patient, if carried on carefully. The performance of phrenicectomy on one side and pneumothorax on the other is not an uncommon procedure. Bilateral pneumothorax is coming into general use and even bilateral phrenicectomy has been performed on a considerable number of patients without deleterious effects. I think it is advisable in bilateral tuberculosis, however, to begin collapse therapy on the side most affected, as this alone is often sufficient to cause healing of lesions in both lungs.

I believe that when collapse therapy is employed in bilateral tuberculosis, the healing of lesions and the closure of cavities in the contralateral lung are due partly to an increased blood supply to this lung, partly to the lessened toxemia and general improvement of the patient when the side most affected is under treatment, and partly to the stoppage of drainage from the cavities. Shifting of the mediastinal structures to this side with the resulting release in tension is also a factor.

It is surprising that it has taken so long to realize what an integral part of the treatment for pulmonary tuberculosis surgical procedures should be. We have all seen many patients in whom nature has attempted to accomplish the same result by shelving the ribs and narrowing the rib spaces, elevating the diaphragm, pulling over the mediastinal structures, etc., in an effort to reduce the volume of the hemithorax by contraction of the fibrous tissue which had been formed in the attempt at healing. To assist this attempt is, in our minds, the sole purpose of surgical procedures.

When a patient with pulmonary tuberculosis is presented for treatment, the first question should be whether or not some surgical procedure might be of benefit. Of course, many patients will be found in whom such measures will not be indicated. If the patients have early, minimal lesions which are improving, it may be decided to give rest in

bed a short trial, or if the disease is far advanced in both lung fields or many complications exist, surgical intervention may seem useless. However, regardless of the result obtained in individual cases, I feel that the mechanics involved clearly indicate that the reasons for employing these measures are fundamentally sound and that until some future scientist discovers a specific cure, the treatment for pulmonary tuberculosis must be surgical, in conjunction with rest in bed and routine methods.

ABSTRACT OF DISCUSSION

ON PAPERS BY DRS. HEDBLOM, BERRY AND O'BRIEN

Dr. Howard Lilienthal, New York; Dr. Hedblom made a convincing point in showing what can be done after the failure of the ordinary posterior thoracoplasty. I heartily approve of this method. I believe that the general method was initiated by Dr. Welles, and I have used it with modification.

Dr. Berry's paper was scholarly and extraordinarily interesting. I had the impression that unfavorable results following the operations for blocking of the phrenic nerve were uncommon. It is most important to bear the possibilities in mind. I certainly shall never again tell a patient that operation on the phrenic nerve can do no harm.

There is another point. In the sequence of operations, I think that it is improper to cause blocking of the phrenic nerve before the establishment of pneumothorax, especially in suppurative disease. In tuberculosis, perhaps, exceptions may be possible, because I have seen the following thing happen: A patient with a bronchiectatic suppuration in the lower lobe had refused to have a lobectomy performed, although she had had the disease a long time, and lobectomy was clearly the best choice. I said, "Let's take out your phrenic nerve."

She said, "Go to it; that's nothing."

I did. I obtained a good elevation of the diaphragm, and the condition of the patient was improved. I said, "Now we will put in some air and get more compression." I neglected to bear in mind the fact that blocking of the phrenic nerve is followed by paralysis and flaccidity of the diaphragm. When Dr. Wessler introduced pneumothorax, he pushed the diaphragm down lower than it was before the operation. I enjoyed Dr. O'Brien's paper, and I am going to read every word of it. He has emphasized an important fact, and that is that there is not an operation for tuberculosis, but that there is a surgical treatment for tuberculosis. The medical profession should be informed on this subject, for nearly every physician thinks only of one operation—thoracoplasty. Concerning the motion of the lungs of which Dr. O'Brien spoke, please bear in mind that the motion of the lungs that one sees when the ribs have been cut is a paradoxic motion. When the patient exhales, his lung expands, and when he inhales, the lung tends to collapse. The picture that was taken on the way to the operating room was undoubtedly taken during full inspiration and this opened the abscess cavity so that it showed very well in the picture. On the way from the operating room the picture was also taken in full inspiration, but the cavity was then closed because the paradoxic motion of the diaphragm and the sucking up of the diaphragm into the chest produced its obliteration temporarily. The abscess cavity was not really and permanently closed.

Dr. E. Archibald, Montreal, Canada: I should like to say a few words concerning Dr. Hedblom's paper. It is timely, I think, that Dr. Hedblom should bring

forward the advantages of the second operation, or perhaps, in Dr. Hedblom's graded plan, the sixth or seventh operation, of anterolateral costectomy.

I failed to gather, however, from his paper that he had made any real distinction between the early and the late operation. He included some cases of pyopneumothorax in which the removal of the ribs anterolaterally would be considered as part of the whole procedure and would therefore be done early, because one cannot close large tuberculous empyema cavities without taking off practically all the ribs from front to back and top to bottom. That has been done for a good many years. He included others, however, in which anterolateral thoracoplasty was performed months or more after the primary posterior thoracoplasty. The distinction is important. The chief indication, I believe, for anterolateral costectomy lies in the group in which there are cavities remaining unclosed by the usual posterior operation. This point was made by Dr. Welles, of Saranac Lake, two or three years ago, in an article in the *American Review of Tuberculosis*. One should be able to judge such cases from the start and say to the patient, "You will not get your cavities closed by the ordinary posterior thoracoplasty. You will need a further stage of the anterolateral type."

I think that is what we should aim at: the conception of an early anterolateral costectomy for patients in whom the cavity is not closed by the posterior operation. I could not gather whether or not Dr. Hedblom intended to make this point in his paper. I have carried it out in a few instances lately. I have performed late secondary operations for years, on the whole without much benefit. Too much fibrosis and reformed bone prevent further collapse, but from this earlier anterolateral costectomy I am getting encouraging results.

Dr. L. T. LeWald, New York: There is a complication that I have seen in a case referred to me by the New York Health Department, in which an operation on the phrenic nerve had been performed the year previously for a tuberculous lesion in the left lung (fig. A). Excessive elevation of the diaphragm followed the phrenicectomy. The patient complained of the same symptoms that I have seen in eventration of the diaphragm which has not resulted from paralysis of the diaphragm in the sense that it is postoperative, but a spontaneous eventration due in some cases to congenital absence of the musculature of the diaphragm; so that the diaphragm being more or less immobile, causes the trapping of gas in the cardiac end of the stomach, and the lower end of the esophagus is below the level of the gas and consequently the patient cannot eruct the gas.

This patient now complains bitterly of the gastric distress so that I feel that occasionally it would be unwise to bring about a paralysis of the diaphragm on the left side.

The slide shows the stomach filled with gas and opaque material, and in the lateral view, the diaphragm can be seen elevated to an enormous height and the stomach below it unable to expel the gas through the esophageal orifice. On the right side, one would not have to consider this complication. I do not know whether this condition has been observed before and whether it is really of sufficient importance to make it unwise to operate unless the condition of the lung is sufficient to warrant the danger of this unpleasant after-result.

Dr. Carl A. Hedblom, Chicago: Dr. Berry's paper is certainly a most important contribution to the subject of phrenicectomy. The operation is generally characterized as simple and harmless, with the inference that it may be performed by operators with meager experience and for slight indications. Dr. Berry's series of cases is large enough to show conclusively that serious complications may result. I have had two patients in whom Horner's syndrome developed. I

am of the opinion that if the nerve cannot be definitely identified without undue effort, it is better to abandon the attempt than to do harm.

The roentgenogram made after the use of iodized oil is an indispensible guide for the prognosis following phrenicectomy. Bilateral involvement seems to me, generally speaking, a contraindication. Cylindrical bronchiectasis, especially of the distal bronchi, in my experience, offers the best prognosis.

The distinction between the terms collapse and compression seems to me of no great importance. In many cases following extensive thoracoplasty there is a decided shifting of the heart toward the opposite side, which would seem to me to indicate that the lung is compressed. We have had cases in which the shifting of the mediastinum has been complicated by pleural effusion. In such cases the manometer has shown positive pressure after thoracoplasty, causing dyspnea and necessitating the withdrawl of fluid.

Eventration of the diaphragm following phrenicectomy.

Dr. Frank B. Berry, New York City: We agree with Dr. Lilienthal as to the advisability of pneumothorax preceding a phrenicectomy in bronchiestasis, as we feel that a great deal of information can be gained and that accidents can perhaps be avoided.

Dr. E. J. O'Brien, Detroit: It seems to me that we are laying too much stress on the dangers of phrenicectomy without bearing in mind just why we are doing it. I do not think that any person would have a phrenic nerve removed instead of going to an afternoon tea. It is removed because the patient has pulmonary tuberculosis or an equally serious disease.

If one accepts the statistics of Naveau, Barnes and others who show that a tuberculous patient with cavity and positive sputum has only a 5 per cent chance of living longer than five years, an occasional accident during the performance of the operation might be excused. I think that we lose sight of the results of the procedure in talking so much about the ill effects.

Readings of intra-abdominal pressure are not as negative as those of intra-thoracic pressure, and one notes intra-abdominal pressure from the viscera in the prone position.

Regarding Dr. Hedblom's observations about the shifting of the mediastinal structures, I have seen that happen time and again under negative pressure during pneumothorax treatment when there could not possibly be compression. When pneumothorax is being administered and the pressure is negative, the mediastinum often shifts. I do not think, therefore, that the shifting of mediastinal structures which occasionally follows thoracoplasty indicates that compression is made by this procedure.

AMEBIC HEPATIC, SUBPHRENIC AND PULMONARY ABSCESSES *

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The occurrence of amebic dysentery in the temperate zones is rare when compared with its occurrence in the tropical zone. It has been only in recent years that the disease has been recognized with any frequency in patients who have not been in the tropics. Amebic abscess is one of the most common complications of amebic dysentery. Rogers [1] stated that acute amebic dysentery usually presents scattered lesions in the bowel and multiple abscesses in the liver. In chronic cases, the lesions are less extensive and may involve only a small part of the bowel. In these cases the abscesses in the liver are usually large and single and the intestinal disorder is often latent, with no clinical manifestations. It is generally accepted that the amebas pass from the ulcerated areas of the bowel, through the portal vein to the liver. In acute cases, amebas in great numbers, often associated with pyogenic bacteria, reach the liver. Inflammation of the vascular walls, clotting and multiple hepatic abscesses result. The occurrence of a large solitary abscess usually is found in cases of slight or latent amebic colitis. Solitary abscesses may be sterile, and their formation differs from the multiple abscess type in that comparatively few amebas reach the liver. When a sufficient number of amebas has reached the liver to cause clotting in some of the small vessels, so that the blood supply is interfered with, sufficient necrosis is produced to permit escape of the amebas through the vascular walls, into the necrotic hepatic tissue, and a solitary abscess is produced. This abscess develops in a concentric manner, and if the patient survives long enough, a fibrous capsule develops around it. It is in the wall of the abscess that the amebas are found. *Endamoeba histolytica* is usually obtained from scrapings from the walls of the cavity, not from the thick pus from the abscess cavity. Rogers found the ameba in the pus in four of eighteen surgical cases in which he conducted the examinations, and in the scrapings of the wall of the cavity in seventeen of the cases.

My experience in the treatment of amebic abscess is limited to five cases in which I have operated in the last five years. My purpose in reporting these cases is to show that although the occurrence of amebic

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1. Rogers, L.: Amoebic Liver Abscess: Its Pathology, Prevention and Cure, Lancet **1**:463, 569, 677 (March 11, 18, 25) 1922; Brit. M. J. **1**:224, 264, 345 (Feb. 11, 18) 1922.

abscess in the temperate zones is uncommon as compared with that in the tropical zone, it is not rare, and also to point out the frequency with which the symptoms in this group of cases of amebic hepatic abscess were thought to be due to primary pulmonary or pleural disease. In the five cases here reported, an initial diagnosis of a pulmonary lesion was made in four. In the fifth case, a definite diagnosis of amebic dysentery was not established until five months after the onset of the disease; an abscess of the liver developed even though the patient was given extensive treatment with emetine.

The usual symptoms in cases of amebic abscess are diarrhea, fever, chills or sweats, occurring some time in the course of the disease. Pain in the right hypochondrium is usually present. Preceding diarrhea is often the only symptom that is significant of the probable etiology. Ludlow [2] stated that it is present in nine of ten cases, although it may have occurred years before the abscess appears. He also wrote, "many of the patients presented a septic condition so often observed in cases of chronic empyema," and he called attention to the special diagnostic sign of deep-seated pain in the region of the abscess, elicited by a sudden thrust with the end of the finger.

In the five cases here reported, four patients gave histories of diarrhea, but in only one case was it a prominent factor in the complaint. In three cases, it was difficult to elicit any history of diarrhea, for the patient had not attached any significance to it and had not mentioned it in stating the history of his complaint at the time of examination. In the remaining case, a history of diarrhea was not obtained.

In one case, the patient contracted amebic dysentery in the tropics. In the remaining four cases, a history could not be obtained of the patients having been out of the north temperate zone. In two cases, there was a history of alcoholism.

The importance of early diagnosis cannot be overestimated, for the prognosis is good if treatment is instituted early, before the additional complication of rupture through the liver and diaphragm into the lung has occurred. In these five cases, the abscess was confined to the liver in two cases, and in both, it was a large solitary abscess. In two cases, the abscess had ruptured through the liver into the subphrenic space. In the remaining case, an abscess presented in the upper lobe of the right lung, which was undoubtedly secondary to an abscess of the liver. It was impossible to determine definitely whether this abscess was the result of direct extension from the hepatic abscess, by rupture through the diaphragm into the lung, or whether the amebic infection was transmitted to the lung through the blood stream, the invading organisms having passed from the hepatic abscess into the inferior vena cava,

2. Ludlow, A. I.: Amebic Liver Abscess, China M. J. **40**:1165 (Dec.) 1926.

to the right side of the heart, and through the pulmonary arteries to the lung. Brown [3] reported a similar case in which he thought that the pulmonary abscess resulted from deposition of amebas by the blood stream, metastatic from the abscess of the liver. This view, he felt, was substantiated at necropsy, because an opening through the diaphragm connecting the liver with the pulmonary abscess was not demonstrable. MacNeal and Klemperer [4] reported a case of amebic abscess which was complicated by multiple small abscesses in both lungs, and from the microscopic examination of the tissue removed at necropsy they concluded that the amebas had a tendency to penetrate the blood vessels and were disseminated by way of the blood stream from the liver, thence to the right side of the heart and pulmonary arteries to the lung. In the case of extension to the lung, which I am reporting, there was response to treatment, and there was no definite way of determining the method of transmission of the amebas to the lung. Nevertheless, the clinical history indicated that extension to the lung was probably brought about by direct transmission through a rupture of the diaphragm.

The surgical treatment should be as conservative as possible and should be combined with adequate administration of emetine. Rogers advocated repeated aspiration and injection of solutions of quinine into the abscess cavity, but omitted the injections of quinine after the introduction of treatment by emetine. He stated that amebic or tropical abscess of the liver is usually an easily preventable disease, and that the occurrence of amebic suppuration in the liver should cause serious consideration by the physician in whose hands it had been allowed to develop.

Ludlow stated that each case of hepatic abscess must be treated according to the condition found, that no hard and fast rule can be made for every case, but that in practically all cases some form of surgical treatment is required besides medical treatment. He also stated that repeated aspirations and subcutaneous injections of emetine is the method of choice, but that in many cases open operation and drainage are required.

The usual procedure is as follows: A preliminary course of emetine (0.06 Gm.) is given by daily subcutaneous injections for from two to four days before operation if the patient's condition will permit delay of surgical intervention. The abscess is then aspirated, the site of aspiration depending on the most likely situation of the abscess, as determined by general examination. The most usual site is the ninth

3. Brown, R.: Amoebic Abscess of Liver with Pulmonary Sequelae, California State J. Med. **19**:282 (July) 1921.

4. MacNeal, W. J., and Klemperer, P.: Amebic Abscess of the Liver, Am. J. Trop. Med. **5**:339 (Sept.) 1925.

interspace in the anterior axillary line. If the location of the abscess is not definitely determined by examination, this site is usually selected for inspiration. The aspirating needle should not be inserted for a depth of more than from 5 to 7 cm. If pus is obtained, a small trocar and cannula is inserted into the abscess, under local anesthesia. A small puncture of the skin with a knife often facilitates the introduction of the trocar and cannula. As much of the pus as possible is removed at the first aspiration. If the pus is thick, a catheter may be inserted through the cannula and the cavity irrigated with a surgical solution of chlorinated soda (Dakin's solution), or it may be necessary to resort to open operation. The aspirations are repeated when the patient shows signs of reaccumulation of pus in the cavity. This depends, to some extent, on the size of the abscess. In large abscesses, there is often rapid reaccumulation of bloody serum after removal of the pus. If the patient does not respond to treatment by emetine, and if the clinical data indicate the presence of an abscess of the liver which cannot be located with the aspirating needle without danger of injury to the lung and pleura, or to the abdominal viscera, it is best to perform exploration of the abdomen. If an abscess is found at exploration, it can be treated either by an open operation or by closing the abdomen without drainage and performing a secondary window operation over the cavity of the abscess for subsequent drainage by aspiration. Subcutaneous injections of 0.05 Gm. of emetine are continued until the patient receives from six to ten doses. This is usually sufficient, but if symptoms recur, a second course of treatment by emetine should be given.

REPORT OF CASES

Case 1.—A man, aged 23, a resident of Indiana, consulted the clinic on June 2, 1928, because of pain in the right lower part of the thorax, of twelve weeks' duration. He stated that his illness began following unusual exposure to cold weather, when pain developed in the right lower portion of the thorax. On the following day, he noticed slight fever but continued to work. There was no cough or hemoptysis, but there was loss of appetite and weight. His condition was thought to be due to tuberculosis, and he was sent to Texas. A roentgenogram of the thorax did not show evidence of tuberculosis, and his condition was then thought to be due to gastric ulcer. He returned home to Indiana and for the three weeks previous to his coming to the clinic had been confined to bed, with severe pain in the upper right portion of the abdomen, lower part of the thorax and right lumbar region. The temperature rose as high as 102 F. in the afternoon but usually did not go above 100 F. He also had occasional night sweats which were severe. He had lost from 20 to 30 pounds (9 to 13.6 Kg.) in weight in the twelve weeks previous to his visit to the clinic. The pain in the right lower part of the thorax had been severe enough for codeine to be required for from two to three weeks prior to examination. He had vomited three or four times and complained of considerable nausea after eating. He was constipated. He had never had diarrhea at any time, and during his illness, had required a daily enema. He was admitted to the hospital as an emergency case.

General examination revealed evidence of marked emaciation. The cheeks were flushed. The margin of the liver was not palpable; there was a slight tenderness in the right upper part of the abdomen and the right lumbar region. Examination of the thorax gave essentially negative information. The systolic blood pressure was 104 and the diastolic, 70 mm. of mercury. The pulse rate was 120 each minute. The temperature was 99.6 F. at 2 p. m. The urine contained a few granular casts and a few pus cells, but was otherwise negative to examination. The concentration of hemoglobin was 64 per cent; erythrocytes numbered 4,010,000, and leukocytes 30,500 in each cubic millimeter of blood. The differential leukocyte count was as follows: lymphocytes, 16 per cent; large mononuclears, 7.5 per cent; transitionals, 2.5 per cent and neutrophils, 74 per cent. The Wassermann reaction of the blood was negative. Repeated examinations of stool before operation did not disclose amebas, ova, pus or blood. A roentgenogram of the thorax gave evidence of marked elevation of the right side of the diaphragm. A diagnois of right subphrenic abscess was made, and exploration was advised.

On June 6, 1928, the right, subphrenic space was found to be negative to several aspirations made through the tenth and eleventh interspaces. Because of the patient's progressive symptoms it was thought best to perform abdominal exploration, and a large, solitary abscess of the liver was found, involving about a third of the right lobe. The hepatic abscess was aspirated, and about 5 cc. of thick, bloody, greenish puslike material was removed. This was immediately taken to the laboratory, and *Endamoeba histolytica* was found to be present. A section of the ninth rib and cartilage were removed, in the anterior axillary line, immediately over the abscess cavity, and a stab wound was made through the posterior periosteum. A strip of gauze was placed in the stab wound and down to the lateral surface of the liver in the abscess cavity. The abdominal wound was closed without drainage. The patient was given treatment by emetine hydrochloride, and on the following day the gauze was removed and the cavity was aspirated through the stab wound in the thoracic wall. About 150 cc. of amebic material from the liver was removed. This was done on three occasions at intervals of three and four days (fig. 1).

There was moderate shock immediately following the abdominal operation. The temperature and pulse were normal on the fifth day, and from that time on convalescence was uneventful. Examination of the stool four days after the operation revealed cysts of *Endamoeba histolytica*. The patient was dismissed from observation one month after operation, at which time he had gained about 20 pounds (9 Kg.), and his condition was good. He had had no fever from the fifth day after operation, and his wounds were entirely healed.

Comment.—The onset, in this case, followed considerable exposure, and suggested pulmonary disease, which was thought probably to be tuberculosis. Tuberculosis was soon ruled out, and the later symptoms were characteristic of subphrenic or hepatic abscess. The patient had not lived outside of the north temperate zone and he had never had any attacks of diarrhea. Although amebic hepatic abscess was suspected clinically, the examinations of stool before operation proved negative for *Endamoeba histolytica*. The preliminary aspiration was performed with the hope of establishing a definite diagnosis without more radical surgical intervention. Aspiration in the right subphrenic and hepatic spaces gave negative results because the abscess was deep

lying, and more anterior than posterior. When exploration of the abdomen was carried out and the diagnosis was established, it was thought best to treat by repeated aspiration rather than by open drainage, because of the danger of secondary infection which takes place under conditions of open drainage, and also because the patient had never received treatment by emetine. It was thought that he would respond more satisfactorily to repeated aspiration than to emetine, and this was substantiated by his rapid response to treatment and his complete recovery.

Fig. 1 (case 1).—*a*, large amebic abscess of the right lobe of the liver; *a'*, site of incision; *b*, resection of the anterior segment of the ninth rib for subsequent aspirations; *b'*, site of incision.

CASE 2.—A man, aged 37, a resident of Michigan, consulted the clinic on Feb. 20, 1929, because of pain in the upper right part of the abdomen, which was referred to the upper portion of the thorax, and because of loss of weight and strength of three months' duration. Four years prior to his admission, while he was in Florida, diarrhea had developed, and he had passed from three to four stools a day. This continued for about four months, when the diarrhea became so severe, associated with blood in the stool, that it was necessary for him to go to a hospital. He had daily rise in temperature; he had lost from 20 to 30 pounds in weight, and had lost strength. Numerous tests had been made, but nothing definite had been found, and his condition was thought to be due to a lesion of the hepatic flexure. One month later, a diagnosis of amebic dysentery was made,

and emetine was administered with immediate response and apparent recovery. Six months later he had recurrence of diarrhea, associated with bearing-down pain in the rectum, weakness and loss of weight. Emetine was again administered with less rapid response. He then continued to have recurrence of symptoms every four or five months. Emetine was given with each attack, but each time the treatment seemed less effective in relieving symptoms. About one year previous to admission, while in Brazil, he had a recurrence of former symptoms, with a temperature of from 100 to 102 F. He was given emetine and chiniofon, N.N.R. and five injections of neoarsphenamine. During this illness, pain developed in the right lower part of the thorax and upper right part of the abdomen. At first the pain was dull. After two weeks, the pain disappeared and the temperature gradually returned to normal. For one month following this, he gained in weight and strength, and after two months he returned to work. Almost immediately after he returned to work, he began to have fever daily; it gradually increased in severity until it reached 104 F. in the afternoon. He was given a course of acetarsone and emetine, with gradual improvement of symptoms, until he felt quite well after a period of three weeks. Four months before he came to the clinic, he suddenly lost appetite; fever again developed, with pain in the right lower part of the thorax and abdomen, moderate diarrhea and gradual loss of weight and strength. This condition had become progressively worse until the time of his admission to the clinic. He had lost 35 pounds (15.9 Kg.) in weight during the four months before his admission.

General examination revealed marked loss of weight. The systolic blood pressure was 94 and the diastolic, 64. The pulse rate was 105 and the temperature was 101 F. Examination of the right side of the thorax disclosed dulness to percussion, anteriorly to the fourth interspace, and posteriorly to the sixth thoracic vertebra. The margin of the liver could be felt from four to five fingerbreadths below the right costal margin, with marked bulging of the lower right portion of the wall of the thorax. Urinalysis gave negative results. The concentration of hemoglobin was found to be 45 per cent; erythrocytes numbered 3,340,000 and leukocytes, 10,600 in each cubic millimeter of blood. The differential leukocyte count was as follows: lymphocytes, 21 per cent; large mononuclears, 1 per cent; neutrophils, 77 per cent; eosinophils, 1 per cent. There was marked anisocytosis and poikilocytosis. Repeated examinations of stool were negative for *Endamoeba histolytica*. Roentgenograms of the thorax gave evidence of marked elevation of the right side of the diaphragm, with some thickening of the pleura (fig. 2*A*). A diagnosis of amebic abscess of the liver was made, and operation was advised.

On February 26, the right subdiaphragmatic space was aspirated through the tenth interspace in the posterior axillary line, and about 2,200 cc. of typical amebic pus was removed from the liver. The fluid was light chocolate-colored, and was streaked with thick puslike material and particles of hepatic tissue. This fluid was sent for examination and was found to be negative on culture. Amebas were not found. Following operation, emetine hydrochloride was given. The abscess cavity was again aspirated, March 4, at which time 800 cc. of the same type of material was removed. The patient did not receive much relief from pain from the second aspiration, and it became progressively more severe. On March 7, a third aspiration was performed with a needle of large caliber, and only a small amount of thick, degenerated material was removed. Because of the patient's poor general condition and the inability to obtain pus by aspiration, it was thought best to resort to open operation. A small portion of the eleventh rib was removed with the idea of draining the subphrenic space. After a segment of the rib had been removed, it was found that the right pleural phrenic space was not oblit-

erated, and that there was a small amount of fluid in the pleural cavity, probably resulting from previous aspirations. It was thought best not to attempt to drain the abscess through the pleural space, and the wound was closed. Abdominal exploration was then performed, and a huge, solitary, amebic abscess was found involving two thirds of the right lobe of the liver. The abscess cavity contained about 500 cc. of thick, bloody, degenerating hepatic tissue. Examination of the scrapings from the wall of the cavity showed *Endamoeba histolytica* to be present. The necrotic material was removed, and the large cavity in the liver was packed with gauze.

There was considerable shock following the operation, after which the patient was given emetine hydrochloride subcutaneously. The gauze was completely removed by the tenth day, after which a tube was inserted and the cavity was irrigated throughout his convalescence with saline and surgical solution of chlorinated soda (Dakin's solution). The patient was dismissed from the hospital on the twentieth day, and from observation about two months after the operation.

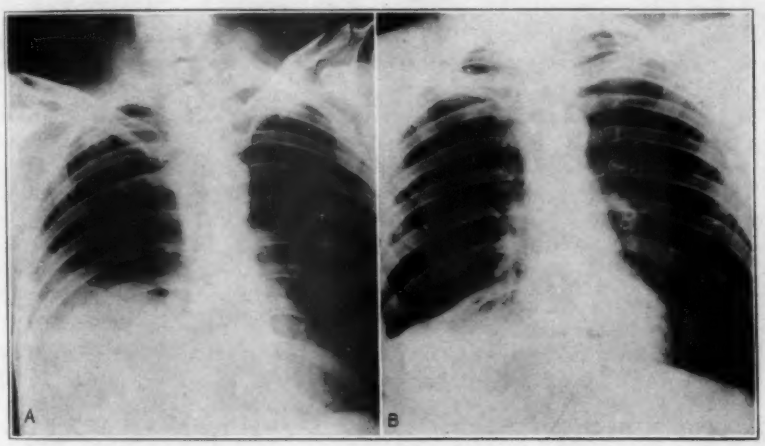

Fig. 2 (case 2).—*A*, roentgenogram on admission showing marked elevation of the right side of the diaphragm with some thickening of the pleura. *B*, roentgenogram on dismissal showing pleuritic adhesions at the right costophrenic angle, and slight elevation of the right side of the diaphragm; the lungs were normal.

At the time of his dismissal, the cavity in the liver had become practically obliterated. There remained a small sinus in the abdominal wall. The patient had gained 25 pounds (11.3 Kg.) in weight, and his general condition was good (fig. 2*B*).

Comment.—The amebic abscess in this case developed in the liver while the patient was under intensive treatment with emetine, and *Endamoeba histolytica* was absent in repeated examinations of stool. It will be recalled that lack of response of the patient to conservative treatment by aspiration and inability to continue it because of the thick, necrotic material in the abscess cavity necessitated the institution of open surgical drainage. However, the costophrenic angle of the pleura was not walled off because the abscess was confined to the liver and

had not ruptured into the subphrenic space. Consequently, abdominal drainage was carried out. From the symptoms, it is evident that the patient had been suffering from abscess of the liver for a year before he came to the clinic. I think it advisable to institute early drainage of the abscess in cases of this type, when the condition does not respond to the more conservative types of treatment.

CASE 3.—A youth, aged 17, a resident of Michigan, consulted the clinic on July 7, 1925, because of pain in the right lower part of the thorax, of three months' duration. He stated that he had been well until about one year before admission when he began to feel tired and to lack ambition. In the last year he had had more or less chronic cough. He had had one severe spell about one year before he came to the clinic. The onset of his present complaint, three months prior to admission, was characterized by cough, fever and a general feeling of malaise. The condition had been diagnosed as influenza, and he had recovered in about a week and had returned to work. He soon had a relapse, with chill, high fever and pain in the right lower part of the thorax. From that time, until he came to the clinic, he had had a constant afternoon rise in temperature, ranging between 102 and 103 F. For ten days prior to admission, he had had nausea, with some vomiting, and the pain had extended into the right flank and right upper quadrant of the abdomen. Pain had been severe at times. He had had considerable urinary frequency, particularly at night, for three to four months previous to his visit. He had always been constipated. On further questioning, after a diagnosis had been established, he stated that he had had one short spell of diarrhea two months previous to admission, with from three to four stools a day over a period of four or five days. He had lost 12 pounds (5.4 Kg.) in weight in the three months before admission.

General examination gave evidence of loss of weight and pallor of skin, indicating a rather marked degree of anemia. The breath sounds over the right base were impaired; there was bulging of the interspaces and marked tenderness of the right lower part of the thorax. Urinalysis gave essentially negative results. The concentration of hemoglobin was 35 per cent; erythrocytes numbered 2,380,00 and leukocytes 12,400 in each cubic millimeter of blood. The color index was 0.5. The differential leukocyte count was as follows: lymphocytes, 27 per cent; large mononuclears, 3.5 per cent; transitionals, 1.5 per cent, and neutrophils, 68.0 per cent. The Wassermann reaction of the blood was negative. Repeated examinations of stool were negative for amebas. Roentgenograms of the thorax gave evidence of elevation of the right side of the diaphragm to the level of the fourth rib anteriorly. Roentgenograms of the colon were negative. A diagnosis was made of subdiaphragmatic abscess of uncertain origin, and operation was advised.

On July 23, the right subphrenic space was first aspirated, and encysted, thick, bloody, greenish material was obtained and was sent for examination and culture, with negative results. Incision was made through the intercostal space, and about 1,500 cc. of thick, bloody, puslike material, with very pungent odor which seems characteristic of amebic pus, was drained from the large abscess cavity. The ameba was found in material scraped from the wall of the abscess cavity. The cavity was packed with a strip of iodoform gauze, and treatment with emetine and acetarsone was instituted.

Immediate convalescence was stormy for the first two weeks, after which the patient's condition began to show some improvement. This, however, was of short duration, and after one week he again began to have an elevated temperature,

with some diarrhea. *Endamoeba histolytica* was found in the stool, and a second course of treatment by emetine was instituted. His general condition again improved moderately, but there was continued loss of appetite and progressive loss of strength. The diarrhea did not respond to administration of emetine or to other treatment. His condition became gradually worse until his death on the forty-fourth day. The cavity of the subphrenic abscess became progressively smaller from the time treatment was begun until his death, at which time it had a capacity of less than 30 cc. At necropsy, it was found that the subphrenic abscess had practically healed. There was marked ulceration of the colon and terminal bronchopneumonia.

Comment.—The course of this patient's illness was insidious and probably extended over several months before the definite event, which simulated influenza, occurred three months before his admission. The periodic attacks of cough, with pain in the right side of the thorax, suggested a primary thoracic lesion, and the recurrence of the attacks suggested a complicating abscess. It was difficult to establish a definite diagnosis because of the absence of any definite history of diarrhea, and because of the absence of *Endamoeba histolytica* in the stool. The lack of response to treatment was undoubtedly due to the extremely bad condition at the time treatment was instituted. The patient's death was due to inanition as result of colitis.

Case 4.—A man, aged 38, a resident of Iowa, consulted the clinic on Aug. 5, 1929, because of morning cough and a draining sinus in the right side of the thorax. Except for chronic morning cough in 1927, he had been well previous to September, 1928, at which time he became ill, and his condition was diagnosed as pneumonia involving the right lung, complicated by jaundice and pleural effusion. Clear, pleural fluid was aspirated many times in the first three weeks of his illness. At the end of the third week the fluid became purulent, and a rib was resected in October, 1928. He had had a draining sinus in the right lower part of the thoracic wall since that time. On second questioning, a more detailed history of his complaint was obtained. He then stated that for three years prior to his admission to the clinic, he had had a cough with a moderate amount of sputum, usually only in the morning. One and a half years prior to admission, he started having spells of weakness which necessitated his stopping work for a day or two at a time. There was gradual loss in weight and strength and progressive morning cough for a period of three months, when he first noted pain in the upper right quadrant of the abdomen. He became jaundiced, and this was accompanied by diarrhea and passage of green, watery stools. For the first two days, he had from ten to twenty stools a day. The stools then became normal and very light and putty-like in color. The condition remained about the same for from six to seven days, when he had sudden pain in the right side of the thorax, severe chills with fever, and marked perspiration which lasted until morphine was given. He was sent to the hospital, and a diagnosis of pneumonia of the right lung was made. The jaundice cleared up in about two weeks, and the stools became colored after about three days. One week after the admission of the patient to the hospital, the right side of the thorax was aspirated, and about 2 liters of clear fluid was removed. The aspirations were repeated every two to three days for the next three weeks, when the fluid became purulent, and one rib was resected for drainage. The patient did fairly well until about one year prior to admission, when he

again began to have fever with slight chills. This subsided with increased drainage from the sinus in the right lower portion of the thorax. He had had repeated similar attacks in the year prior to his visit to the clinic, which would disable him for from a few days to a week at a time. The bowels were normal, and he had no cough or expectoration in the year previous to his admission. He had lost 60 pounds (27.2 Kg.) in weight during the year.

Results of general examination were essentially negative, except that it disclosed marked loss of weight and abnormalities in the right side of the thorax. The urine was normal. The concentration of hemoglobin was 35 per cent; erythrocytes numbered 3,800,000 and leukocytes 7,400 in each cubic millimeter of blood. The color index was 0.6. The Wassermann reaction of the blood was negative. Examination of the pus discharged from the sinus of the right side of the thorax did not disclose sulphur bodies or actinomycosis. Roentgenograms of the thorax revealed evidence of elevation of the diaphragm on the right side with a fluid level beneath, suggesting an old subphrenic abscess. Operation was advised.

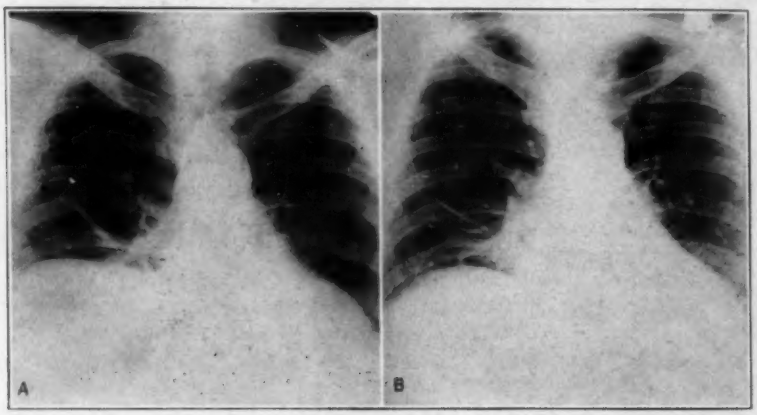

Fig. 3 (case 4).—*A*, roentgenogram on admission showing fluid at the base of the right lung apparently below the diaphragm; the fluid level at the tenth rib, posteriorly; partial collapse of the lower right lobe and enlargement of the heart, graded 1. *B*, roentgenogram on dismissal showing moderate elevation of the right side of the diaphragm and slight interlobar pleurisy; the lungs were normal.

However, the patient refused to be operated on and went home. He returned to the clinic on December 30, as his condition had been getting progressively worse since his previous visit (fig. 3*A*). He had been unable to do any work in the interval.

On Jan. 4, 1930, a tube was inserted into the draining sinus in the right lower part of the thorax, and about 700 cc. of reddish-brown, thick, purulent material, with fetid odor, was removed. This was found to contain *Endamoeba histolytica*. Drainage of the subphrenic abscess was established in one stage by resection of 7.5 cm. of the tenth and eleventh ribs in the posterior scapular line. The cavity held about 900 cc. of this same reddish-brown, purulent material. On exploration of the cavity, it was found that the sinus tract, which led to the right lower lateral thoracic wall was very tortuous and opened into the extreme anterior angle of the subphrenic abscess, at which point it had penetrated the diaphragm.

Convalescence was uneventful. The temperature dropped to normal on the fourth day. The patient was dismissed from the hospital on the fourteenth day, at which time the wound was in excellent condition, and there was a large residual cavity which was filling in rapidly. The patient was dismissed from observation six weeks after the operation, at which time the cavity was almost completely obliterated, and his general condition was excellent. He was given two courses of emetine during convalescence and had gained 15 pounds (6.8 Kg.) in weight, with marked increase in strength. He returned for observation three months after operation, at which time his general condition was very good. The concentration of hemoglobin was 60 per cent, and he had gained 40 pounds (18.1 Kg.) in weight. The operative wound and the old sinus in the anterior thoracic wall had

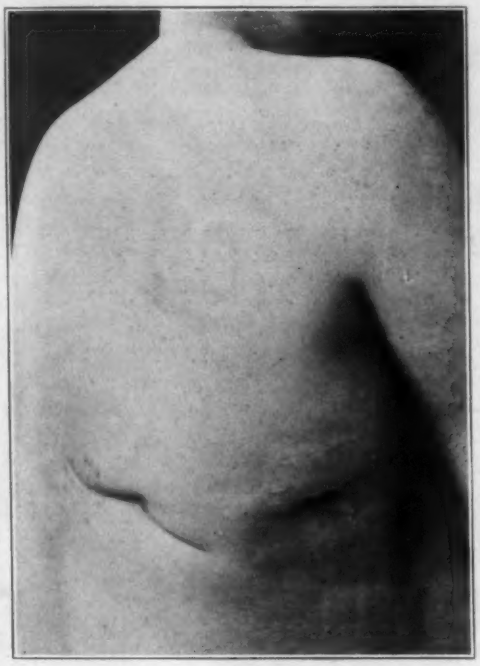

Fig. 4 (case 4).—Old sinus in the right side of the thoracic wall, and recent operative wound entirely healed on patient's dismissal; condition excellent; gain of 40 pounds in weight.

entirely healed. The roentgenogram of the thorax gave evidence of elevation of the right side of the diaphragm to the fourth rib and did not reveal abnormality in the lungs (figs. 3*B* and 4).

Comment.—This patient stated that he had always lived in a temperate zone and had never been south of Iowa. He had been troubled more or less with diarrhea since he was a small child, and therefore attached no significance to the more recent attacks of diarrhea. The severity of his illness, simulating pneumonia, is rather unusual. Probably the original condition was abscess of the liver which had

ruptured into the subphrenic space, at that time causing the marked prostration. The progressive dyspnea probably resulted from a complicating pleural effusion due to the subphrenic abscess. The first aspirations undoubtedly drained this secondary clear pleural effusion. The later aspirations probably penetrated the diaphragm. Then, as resection was of the ninth rib in the midaxillary line, and as the diaphragm was markedly elevated, the subphrenic space was entered instead of the pleural cavity, and thus the extreme anterior portion of the abscess cavity was drained. Open surgical drainage was necessary because of the secondary infection of the amebic abscess and because of the patient's extreme illness.

Case 5.—A man, aged 25, a resident of Indiana, consulted the clinic on Dec. 6, 1928, because of loss of weight and hemoptysis of five weeks' duration. About three months prior to admission, he noticed pain in the right posterior portion of the thorax, with afternoon fever, loss of appetite, general weakness and loss of weight. A week or so later he first noticed a nonproductive cough. About two months before he came to the clinic, after he went to bed, he coughed up some blood. He consulted a physician, and a diagnosis of fluid in the right side of the thorax was made. Diagnostic aspiration was done, at which time a small amount of bloody, purulent material was obtained. A few days later, resection of a rib, with drainage of the right pleural cavity, was done. There was some improvement in his condition, but the cough continued, became progressively worse, and was accompanied by considerable bloody expectoration. There was little drainage from the thoracotomy wound, which had practically closed. Because of his cough, bloody expectoration and loss of weight, a malignant condition of the lung was thought to be present.

At the time of admission to the clinic, the patient was weak and emaciated, and was sent immediately to the hospital. He stated that previous to the onset of pulmonary symptoms, he had had loose, watery stools, probably three or four times a day. He did not think much about this. There was no pus or blood in the stools. While in the hospital, six weeks before he came to the clinic, his condition had become worse and had remained so for four weeks while he was there. On dismissal, two weeks before he was seen at the clinic, his condition was improved, but his symptoms recurred on admission to the hospital after he had come to the clinic.

General examination revealed marked emaciation, with loss of about 35 pounds (15.9 Kg.) in weight. The systolic blood pressure was 120, and the diastolic, 80. The pulse rate was 150, and the temperature at 4 p. m. was 101 F. Examination revealed dulness, with decreased breath sounds and decreased fremitus over the entire right side of the thorax, posteriorly. There was a healed scar in the right side of the thorax, posteriorly. Urinalysis gave essentially negative results, except that it revealed a few pus cells. The concentration of hemoglobin was estimated at 45 per cent; erythrocytes numbered 3,310,000 and the leukocytes from 14,800 to 28,100 in each cubic millimeter of blood. Examination of the sputum for bacilli of tuberculosis, spirilla and fusiform bacilli gave negative results. The stool contained *Endamoeba histolytica*. Roentgenograms of the thorax revealed evidence of a thickened pleura at the right base, with a fluid level at the fourth rib (fig. 5*A*). A diagnosis was made of amebic abscess of the lung, secondary to a ruptured abscess of the liver, and operation was advised.

On December 8, the right thoracic cavity was aspirated, and a small amount of thick, bloody, greenish pus was removed. This was found to contain *Endamoeba histolytica*. The stool obtained on the same day contained *Endamoeba histolytica*. Two courses of emetine and a product similar to acetarsone were given. The patient's condition immediately began to improve. He continued to have considerable cough and expectoration, and roentgenograms of the thorax disclosed a shadow in the region of the right lower lobe, posteriorly. It was thought that this was either a walled-off pocket in the pleura or an abscess of the lung, and operation was advised. On December 15, posterior thoracotomy was performed, and a small pleural pocket containing about 30 cc. of thick, purulent material was found, into which opened several bronchial fistulas, with a large necrotic mass in the right middle lobe of the lung. A portion of this necrotic pulmonary tissue was removed for better drainage, and the cavity was packed with iodoform gauze. The necrotic material removed from the wall of the abscess in the lung contained amebas. Two subsequent courses of the aforementioned drugs were given.

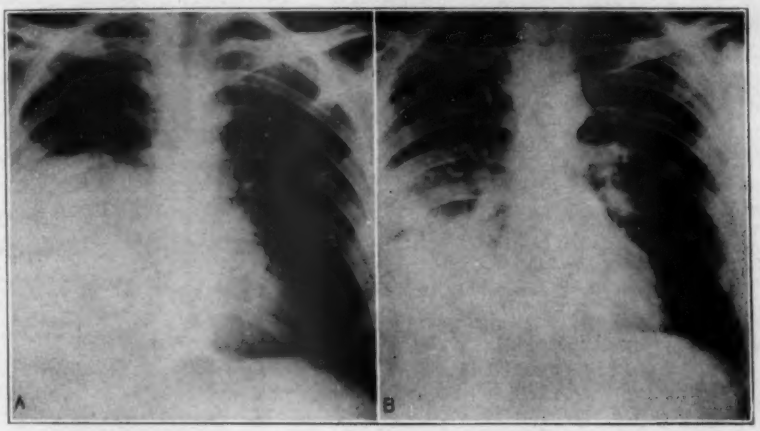

Fig. 5 (case 5).—*A*, roentgenogram on admission showing increased density over the entire lower right portion of the thorax; elevation of the diaphragm (?); fluid (?). *B*, roentgenogram one month after drainage of an amebic abscess in the lower portion of the right lung; dense infiltration of the base, and elevation of the right side of the diaphragm.

The patient's condition continued to improve satisfactorily. He was dismissed from observation on the forty-eighth day after operation, at which time his general condition was satisfactory. He had gained 26 pounds (11.8 Kg.) in weight and there was marked improvement in strength. The thoracotomy wound had practically healed. A roentgenogram of the thorax disclosed dense infiltration at the right base and elevation of the right side of the diaphragm (fig. 5*B*).

Comment.—This case was diagnosed, successively, as primary intrathoracic disease, empyema and a malignant condition of the lung. The attack of diarrhea at the time of the patient's admission to the clinic suggested the possibility of an amebic abscess of the liver which had ruptured through the diaphragm. It is unusual to find amebas in the pus which is removed from the thoracic cavity.

ABSTRACT OF DISCUSSION

DR. L. T. LEWALD, New York: I should like to show several slides illustrating the difference between a subphrenic lesion and a pleural lesion.

In the case (for a report and illustration of the case see Subphrenic Abscess and Its Differential Diagnosis Roentgenologically Considered, ARCH. SURG. **10**: 544 [Jan.] 1925) illustrated in this slide I had previously examined the patient on account of a subacute abdominal condition on the right side, which may have been due to appendicitis. About a month later, I saw this large fluid level lesion with some irregularity just above it. My diagnosis was subphrenic abscess associated with slight pleuritic involvement, simply adjacent irritation through the diaphragm without any actual collection of fluid in the pleural cavity. I had great difficulty in maintaining this diagnosis. Two internists insisted that the fluid was in the pleural cavity. Two surgeons also said the fluid was in the pleural cavity. However, one surgeon agreed with me that it was a subphrenic abscess, which proved to be the case.

I was particularly convinced by the lateral thoracic view, with a complete curve of the diaphragm, that the fluid was below the diaphragm. I think that makes the differential diagnosis with absolute certainty. The dome of the diaphragm is perfectly depicted following this line all the way back, and above that the slight pleural exudate on the diaphragmatic surface of the pleura.

At the first operation, the surgeon who was not convinced that it was a subphrenic abscess did an open operation above the diaphragm and then inserted a probe with the idea that it would lead into the abscess cavity. It did not, but went into the pleural cavity. However, it did no harm, as the pleura was already infected. Then at a subsequent operation an incision was made downward through the diaphragm, and the abscess was drained.

Drainage was then instituted, and the patient made an excellent recovery. I took a roentgenogram of him several months afterward, and the diaphragm remained slightly elevated, but the pleural lesion had entirely cleared up.

I insist that direct lateral exposure is necessary in making a differential diagnosis in a case of this sort. If oblique prejection is used, the signs are difficult to interpret. Oblique projection is useful at times and supplemental, but to see the dome of the diaphragm it is necessary to make a direct lateral exposure.

THE TREATMENT FOR PENETRATING WOUNDS OF THE PLEURAL CAVITY*

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ST. LOUIS

The treatment for wounds that penetrate the pleura is diametrically opposed in many respects to the treatment for wounds that penetrate the peritoneal cavity. The treatment for wounds that penetrate the abdominal cavity usually is radically operative; for those wounds which penetrate the thoracic cavity, the conservative nonoperative treatment is often the best. The presence of blood within the abdominal cavity is of little moment. It may be left undisturbed. Blood left within the pleural cavity may lead to extensive empyema and death.

The surgical principles that govern the treatment for wounds of the peritoneal cavity cannot be applied to the treatment for wounds of the pleural cavity. This distinction is important. It saves life. If the surgeon performs an exploratory thoracotomy on the same premises that he does an exploratory laparotomy, for example, for a penetrating gunshot wound, many patients whose chests are explored will die who otherwise would not have died.

The explanations for this are based on five facts: 1. There are differences between the organs contained within the pleural, and those within the abdominal, cavity. 2. The pressures within the pleural cavity are maintained at a more negative level than are the pressures within the abdominal cavity. The natural tendency of the pleural cavity is toward the formation of cavities; the natural tendency of the abdominal cavity is toward their obliteration. 3. The pleural cavity seems to react to the presence of contaminated blood in a manner different from that of the peritoneal cavity. 4. It is impossible to bring the pleural cavities and the organs that they contain to a complete or even an effectual rest. 5. The blood pressure within the pulmonary circulation is only one-sixth the pressure within the systemic circulation. Bleeding is more easily controlled when it occurs from the pulmonary system than when it occurs within the abdominal cavity.

The recent World War afforded an unusual opportunity for the study of penetrating wounds of the chest. For the first time the modern surgeon, equipped with his present knowledge, could observe and treat such wounds in wholesale lots. Large defects in the chest wall were often seen as the result of shrapnel and pieces of high explosive

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shells. Of course, there were numerous bullet wounds of the chest that produced injuries similar to those met with in civil, or perhaps uncivil, life today.

In the beginning of the war, wounds of the chest that did not produce immediate death were not considered unusually serious. This idea was the result of previous experiences with wounds observed in civil life. It was soon found, however, that the wounds resulting from shrapnel and high explosive shells were different from the wounds seen in civil practice.

Bradford,[1] one and a half years after the beginning of the war, reported a series of about 500 cases of gunshot wounds observed in a base hospital. The patients were first seen by him from two days to one or two weeks after injury. Such cases, he found, were not attended by a high mortality. He noted that 25 per cent of all cases of hemothorax following penetrating gunshot wounds showed infection. He advocated aspiration of the hemothorax and simultaneous replacement of the volume withdrawn by oxygen. The present report shows the beneficial effect of removal of the hemothorax, but the method of removal differs slightly from that used by Bradford. He found only 1 case in which there was a fatal secondary hemorrhage in 500 cases of gunshot wounds.[2]

Duval [3] collected from the literature a total of 3,453 cases, reported by 37 authors. These wounds of the chest and lung were sustained in the war. The mortality was found to be 20 per cent. He found that hemorrhage and asphyxia due to large defects in the wall of the chest were the principal causes of early death.

Certain definite procedures of treatment were evolved, both in the Allied Armies and in the Armies of the Entente. Duval and his co-workers established elaborate surgical procedures for the treatment of extensive wounds of the chest. This was essential to the treatment for war wounds. In these cases the defect in the chest wall is often large and the wound in the lung is extensive. These conditions seldom obtain in wounds of the chest acquired in civil life.

Duval noted that simple bullet wounds were either immediately fatal or relatively benign. It is important to recognize this in civil practice. Experience leads one to believe that it is seldom necessary to operate on the ordinary gunshot and stab wounds of the pleural cavity.

It is not my primary purpose in this paper to discuss the treatment for war wounds of the pleural cavity. The foregoing comment was

1. Bradford, John Rose: Gunshot Wounds of the Chest, Lancet **1**:227, 1916.
2. Bradford, J. R.: Brit. J. Surg. **3**:247, 1915.
3. Duval, Pierre: Les plaies de guerre du poumon, Paris, Masson & Cie, 1917.

made for the purpose of contrasting such treatment with that necessary in the usual penetrating gunshot and stab wound met with in civil life. Admirable descriptions of the proper treatment for war wounds of the chest have been published by Lilienthal,[4] Duval,[3] Rudolf,[5] Gask and Wilkinson,[6] and Roberts and Craig.[7]

Among the many other excellent articles dealing with the proper treatment for war wounds, those of Lockwood,[8] Dobson,[9] Morelli,[10] Hutchinson,[11] and Tuffier [12] summarize the treatments for the various types of injuries.

PRESENT SERIES

This is a report of the study of 162 cases of gunshot and stab wounds of the chest. These patients had entered the Barnes Hospital or the St. Louis City Hospital shortly after they had sustained their injuries. They were all seen within the first four hours after injury except for two patients who entered the Barnes Hospital twenty-four and thirty-two hours, respectively, after injury.

Following these penetrating wounds of the pleura, death occurs as a result of the immediate effect of bleeding and also as a result of the later complications. Foremost among the later complications is empyema.

Several years ago, during an investigation of the etiology of empyema, I had occasion to observe a number of gunshot and stab wounds of the pleural cavity. My experimental work indicated that the presence of contaminated blood within the pleural cavity is likely to lead to the formation of empyema. From this experimental work I acquired a great deal of respect and concern for contaminated hemothorax. In

4. Lilienthal, Howard: Thoracic Surgery, Philadelphia, W. B. Saunders Company, 1925, vol. 2, p. 518.

5. Rudolf, R. D.: Later History of Cases of Gunshot Wounds of the Chest with Retained Missiles, Lancet **2**:709, 1917.

6. Gask, G. E., and Wilkinson, K. D.: Penetrating Gunshot Wounds of the Chest and Their Treatment, Brit. M. J. **2**:781, 1917.

7. Roberts, J. E. H., and Craig, J. G.: The Surgical Treatment of Severe War Wounds of the Chest, Brit. M. J. **2**:576, 1917.

8. Lockwood, A. L.: Early Operative Treatment in Chest Surgery, War Med. **2**:6, 1917-1918.

9. Dobson, J. T.: Some Features of Gunshot Wounds of the Chest, Brit. M. J. **1**:661, 1918.

10. Morelli, Eugenia: Contributo alla cura dell'empiema, Policlinico (sez. med.) **25**:153, 1917.

11. Hutchinson: A Study of 450 Cases of Wounds of the Chest, with Special Reference to a New Method of Treatment for Infected Haemothorax, Canad. M. A. J. **8**:972, 1918.

12. Tuffier, T.: The Secondary Surgical Treatment of Chest Wounds, War Med. **2**:16, 1917-1918.

every gunshot or stab wound of the pleura that I observed there was opportunity for the formation of a contaminated hemothorax. My efforts were directed, therefore, toward the prevention and removal of the hemothorax.

The idea of removal of the hemothorax is not new. It is practiced generally. During the World War it was found that the mortality was reduced about 15 per cent by careful attention to aspiration of the blood. A curious fact is that the blood does not clot readily within the pleural cavity. I have been able to aspirate blood as long as nine weeks after a patient received a gunshot wound of the chest.

There is a more simple way of removing the blood from the pleural cavity than by aspiration. It consists of closing of the wound in the wall of the chest and having the patient lie with the closed hole down, in the most dependent portion of the chest. The hemothorax will gradually leak out.

The following case is an example:

REPORT OF A CASE

S. C., entered the hospital on Oct. 28, 1923, at 10:50 p. m., with a history of having been shot with a pistol one-half hour before. He was conscious, bleeding from the mouth and thirsty. He answered questions intelligently.

On examination, a small round wound was visible in the lower portion of the right axilla at the level of the sixth rib. There was a larger wound in the midsternal line at the level of the third rib through which air was being sucked with each respiration. There was no marked bleeding from either wound. (The patient was lying on his back.) The pulse rate was 120, respirations 24 and temperature 37.4 C. (99.3 F.).

Fluoroscopic examination of the chest showed the side to be clear. The cardiac outline was not markedly enlarged; the shape of the pericardium was that of a normal heart. The right side of the chest was opaque throughout. When the patient was turned on the left side he complained of shortness of breath and the heart shadow moved toward the left. Hemothorax (and pneumothorax) of the right side of the chest was evident.

The percussion note was resonant in the left side of the chest. The coin sound did not indicate pneumothorax of the left pleural cavity. The right side of the chest disclosed distant breath sounds, with some impairment but no flatness.

Immediately on the patient's entrance to the hospital he was given hypodermoclysis of 1,000 cc. of physiologic solution of sodium chloride. The sucking wound of the chest was closed. He was turned on his right side and kept with the bullet wound down. Morphia, ⅙ grain, was given, and the dose was repeated during the night.

At 2:30 a. m., on October 29, the patient was found to be bleeding profusely from the wound beneath the right axilla. A pressure bandage was applied (note by Dr. Deakin). At 3:30 a. m., he was still bleeding from the wound in the chest wall (Dr. Deakin). During the night the temperature rose to 103.6 F. At 8:00 a. m., examination showed the blood pressure to be 98 systolic and 40 diastolic; the temperature was 39.6 C. (103.1 F.) and the pulse rate 122. The rate of respiration was 40. The respirations remained stationary, the blood

pressure had fallen, and the pulse rate remained stationary. On the same day Dr. Singer saw the case and made the following note: "There is no evidence of hemothorax. Considerable interstitial emphysema throughout the right chest extending down to abdomen. Left lung is clear." A transfusion of 500 cc. was given. The patient's temperature became normal on the third day and did not rise again.

The discharge note made by Dr. Webb, on November 10 stated: "Patient was brought in suffering from gunshot wounds of the chest through the lungs; much hemorrhage took place. A blood transfusion was done. He recovered somewhat rapidly and was apparently well on discharge."

Comment.—The striking feature in this case was the absence of hemothorax on the morning following the injury. There was a marked hemothorax one hour after the injury, but this leaked out. The course was unusually smooth, while the patient was in the hospital, and the condition cleared up rapidly. He was given a transfusion on the morning following his entry to the hospital, but the red blood cell count indicates that this was not urgently necessary. The fact that he had eliminated

Laboratory Observations

Date	Red Blood Cells	Hemoglobin, per Cent	White Blood Cells
November 29.....	3,540,000	60	7,200
November 30.....	3,600,000	60	11,800
November 31.....	4,200,000	70	6,100 } (two counts 5,900 } made)

the hemothorax and that blood was visible on the dressings gave rise to the belief that he had had an unusual amount of hemorrhage, and a transfusion was therefore given for safety. After the first day the temperature was never above 100 F.

By thus allowing the blood to escape slowly from the pleural cavity, the formation of an extensive hemothorax is prevented. This procedure was used as a routine measure in thirty-eight cases. None of the patients died. In six of the thirty-nine cases sufficient blood remained in the pleural cavity to justify aspiration.

The clinical course in patients who are kept free from the formation of an extensive hemothorax is smooth. They are almost free from fever, respirations are not labored, there is little shock and sweating, and the patient feels comfortable. In four cases, transfusions were made on account of loss of blood.

There has been a question in my mind from the beginning of this work as to whether it is wise to allow the escape of a hemothorax early after injury to the lung, since its presence is considered to be beneficial in reducing the hemorrhage from the lung. It seems logical to expect collapse of the lung to be beneficial in controlling hemor-

rhage from it. However, there was no clinical evidence in the thirty-eight cases observed that the gradual and continuous escape of the blood from the pleural cavity increases the hemorrhage from the lung.

It has seemed to us that the gradual escape of the blood from the pleural cavity has certain desirable features that recommend it in preference to aspiration. In the first place, the leakage is continuous and slow, while aspiration is done rapidly and at intervals. Aspiration produces a sudden expansion of the injured lung which would be expected to lead to hemorrhage. If the blood is allowed to leak out gradually as it escapes from the injured lung, no sudden change in the contour or size of the wound in the lung is brought about. Then, too, the escaping blood serves as an index to the amount of bleeding that is taking place. One can see it; 50 or 100 cc. of blood produces considerable soiling of the dressings. In contrast to this, much larger quantities may accumulate within the pleural cavity without their presence being noted. Frequent roentgenograms made with the chest in the upright position will reveal this blood. This, however, is difficult to accomplish. If the formation of a large hemothorax is prevented, the patient remains free from fever, he is comfortable and convalescence may be said to begin at once. With an extensive hemothorax, even if sterile, the patient is usually sick and often has a temperature reaching 103 F. Finally the presence of a hemothorax is conducive to the establishment of an empyema. It should not be allowed to remain.[13]

RESULTS

Of the 162 cases reported here, 47 were stab wounds, and 115 gunshot wounds, of the chest. Seven of the cases of stab wound proved fatal, but the cause of death was associated stab wounds of the abdomen in 5 cases and immediate hemorrhage from the heart in 2 cases. No patient died of injury to the lung. Hemothorax occurred in 42 of the 47 cases. Two patients were operated on for ligation of the intercostal artery. The pleural cavity was not explored in either of these cases.

In the 115 cases of gunshot wounds of the chest, only 5 patients died when the pleural cavity only was entered by the bullet. Two of these died immediately of hemorrhage, and 3 died later as a result of infection of the pleural cavity and injured lung. A total of 27 of the 115 patients died. Twenty-two of these cases were complicated by associated wounds of the abdomen, spinal cord and skull. It is evident that patients with ordinary bullet wounds of the chest usually survive unless there are associated wounds which cause death.

13. Allen, D. S.: The Etiology of Empyema, Surg. Gynec. Obst. **45**:23, 1927.

One of these patients died from associated injury of the left ventricle. This was correctly diagnosed, and the mediastinum was immediately explored. The apex of the heart was found to have been shattered by the bullet to such an extent that it was impossible to check the hemorrhage.

Bullets were removed from 21 of the 115 patients with gunshot wounds. In 15 cases the bullets were embedded in the wall of the chest and could be removed without disturbance of the lung. In 6 cases the bullets were removed from the lung, but in no instance before two weeks had elapsed after the injury.

COMMENT

The treatment for gunshot and stab wounds of the pleural cavity has been directed, in the main, toward removal or prevention of the formation of a hemothorax. It was not found necessary to operate immediately on the lung in a single instance. Only 7 of the 135 patients died who had penetrating wounds involving the chest only. Three of these died from hemorrhage from the heart. This low mortality rate in patients with simple stab and gunshot wounds of the pleural cavity indicates that it is seldom necessary to explore the chest in such cases.

The methods employed to deal with the hemothorax were: simple aspiration, aspiration and immediate replacement of the aspirated blood by air; and, in thirty-eight cases, allowing the blood to leak out of the closed wound in the wall of the chest. In two of the latter thirty-eight cases, air was injected into the pleural cavity to allow for collapse of the lung; following this, the patient was placed with the closed wound down. The hemothorax gradually leaked out. This method of dealing with a hemothorax seems to be as logical as aspiration and the simultaneous introduction of air for replacement.

I wish to emphasize the fact that the commonest wounds of the chest, as they are met with in civil life, differ in type from the extensive wounds met with during the World War. Those occurring in civil life are usually the result of pistol bullets and stabbing with a knife. They seldom require surgical exploration of the pleural cavity.

ABSTRACT OF DISCUSSION

DR. A. T. BAZIN, Montreal, Canada: I was very much interested in Dr. Allen's presentation, particularly in that which is new to me, the ability of getting rid of a hemothorax by placing the patient on the wounded side. Collected blood in the pleural cavity clots slowly. Later it liquefies and aspiration of it can be maintained for a considerable period of time.

He has dealt with the most benign type of wound of the chest, gunshot wound. I think that Duval developed the radical treatment more for ragged wounds, shell wounds, with wide open gaping wounds in the chest wall. In my first two years of war service I was in the field ambulance. We learned, and in fact later were

ordered, to close these gaping wounds immediately with anything. The patient's condition immediately improved. Large doses of morphine were given frequently, and the patient was kept in a sitting position until he could be moved. My last year of service was at the base hospital, where there was a fairly large hut in which wounds of the chest were treated. There we met with cases of hematoma with gunshot wound.

There is one point that I should like to emphasize. As Dr. Allen suggests, if the cases are seen late, a hemothorax will not leak out after the wound is more or less sealed over. Something has to be done with the hemothorax. They can be classified as large and small. A small hemothorax, no broader than the hand may be let alone, with the patient sitting up, and no evil results will happen. I used to aspirate the large hemothorax.

Another classification is noninfected and infected hemothorax. We found, by collaboration with our pathologist, Laurence Rhea, that we could anticipate the infection of the hemothorax and deal with it accordingly. In routine aspirations, every second day, cultures were made of the aspirated material; the fluid was spread out on a plate and little portions of clot could be picked out. These were crushed under a cover slip and stained, and occasionally one would find in those little pieces of clot definite colonies of organisms. As soon as that was discovered, the case was ready for operation, thoracotomy, thorough cleansing of the hemothorax and complete closure in layers, an airtight closure, with subsequent repeated aspirations. Under such treatment massive empyema or any severe infection in the pleural cavity was avoided. Getting rid of the residuum of clot, which is an excellent culture medium for the organisms, produced a comparatively mild infection of the pleural membranes.

Dr. D. C. Elkins, Atlanta, Ga.: During the last year in Atlanta I had ninety-six cases of penetrative wounds of the chest, all occurring in Negroes. The great majority of them were due to ice pick wounds, a few to razor wounds and the rest to gunshot wounds. Of the ninety-six patients, eight died—seven of them within twelve hours—of extensive lesions, usually complicated by gunshot wounds of the abdomen, spinal cord, bladder or brain. In three of the eighty-nine patients who lived, empyema developed; one of these died of a staphylococcic septicemia, and in the other two patients chronic empyema developed that was exceedingly difficult to clear up.

Our method of treatment was to give all of the patients large amounts of morphine, to close the external wound when they were "sucking" and to begin the aspiration on the third to the fifth day; it was our opinion that if the fluid was left alone that long, it would compress the lung, as Dr. Lilienthal said, and prevent further bleeding, and that after that time there would probably be no bleeding after the aspiration.

I was much interested in what was said in regard to placing these patients on the side for drainage. I shall certainly try it.

Dr. C. D. Lockwood, Pasadena, Calif.: I think that this article of Dr. Allen's is timely, not only from the point of view of gunshot wounds, but from that of the number of crushed chests that are seen in automobile accidents and particularly in airplane accidents.

I agree more or less with what Dr. Bazin and Dr. Lilienthal said in regard to the treatment in some of these cases. In the group of cases in which Duval undoubtedly first started his operation the patient otherwise died in advanced operating centers or in the casualty clearing station and was never sent to the base area at all. These patients had a wide open chest with an extensive hemo-

thorax, the opening of which was so wide that it could not be kept closed by suture or by adhesive plaster. The patient died within an average of from twenty-four to forty-eight hours. Those who reached the casualty clearing station alive were dead within usually forty-eight hours. This occurred until July, 1916. For a year and a half I had made a practice of observing cases of this type every day and consigning a certain portion of them to a moribund ward. The patients were given morphine and left to die. Beginning with the last week of July the mortality of 80 per cent in that group was changed to 33 per cent for twelve months out of the year.

That type of procedure applied to cases of a wide open chest in which there was no hope of saving the patients except by radical measures. In these gunshot wounds of the chest one has to keep in mind one or two of the problems of which Dr. Allen spoke, particularly that of whether or not the wound is a ragged type that might have carried some clothing into the chest. In this case an infected hemopneumothorax would occur; on the other hand if it is a clean type of bullet wound, with a small hemothorax, and if the patient is getting along fairly comfortably, one should wait for some time. We have made the rule, however, that these patients should be looked on as emergency cases day and night, that the physician in charge of that work should be called immediately when the patient's condition seems to require it, and that he should constantly observe the patient for the first six to eight hours. When the patient does not improve gradually, we give him a transfusion and get ready for the operation. We would not aspirate the chest under any conditions at that time, but we might attempt to put more air into the chest as Dr. Lilienthal has said.

For five years I have been taking a rather active interest in the flying corps in my country, and we have rather active clubs there at the present time. There is a rule that all flyers carry a small emergency kit, so that if a flyer crashes and has an open wound in the chest, it can be sewn, if possible, or covered with adhesive tape. Besides this they are provided with the ordinary first field dressing used during the war and with a small ampule of morphine tablets to take by mouth. By tiding them over with morphine and by closing the opening in the chest we hope to prevent the mortality that occurs in these cases in the first half hour. If the patient reaches the hospital, even though he has a badly staved-in chest we may be able to do something for him.

We deal with these cases as we did during the war. We watch the patients closely, and if they are not holding their own and have a large hemothorax, we prepare to operate on the chest. I think that one must follow the same procedure with gunshot wounds if the patients are not holding their own at the end of about six hours. If they have a clean bullet wound, I think that they ought to be let alone. They ought to be given the benefit of any doubt, however, and operated on rather than be let alone.

DR. F. T. LORD, Boston: I should like to suggest in addition that the cultures be made under anaerobic as well as aerobic conditions.

DR. H. BRUNN, San Francisco: I believe that all are agreed that the conservative or expectant method of treatment is, in general, the preferable course to follow in the treatment for penetrating wounds of the chest. It has been my experience, however, that this method of treatment does not answer the question for all cases. When death occurs the question arises as to whether or not more active measures taken earlier would not have been the better policy. I feel, therefore, that careful observations must be made on every penetrating wound in its earlier stages in order to decide if the hemorrhage is uncontrolled and if a radical procedure is indicated.

In looking over statistics at the San Francisco Hospital for a period of ten years and following up some of the cases, we discovered that while patients were discharged as cured they were left disabled because of inability to resume their usual occupations. This was usually the result of adhesions which caused a great diminution in their vital capacity.

As a result of these observations we adopted in our conservative measures a certain line of treatment. As soon as fluid collects in the pleural cavity it is withdrawn and an equal quantity of air is put in with a pneumothorax machine and the pressure read. We do not remove fluid without replacing with air. By this means we are enabled to remove the fluid early without setting up the hemorrhage afresh by the release of pressure. We also believe that fluid in the pleural cavity is defibrinated by the churning action of respiration and that this deposit of fibrin early covers the parietal and visceral pleura and quickly becomes organized, fixing the lung in an unnatural position.

Our policy, therefore, is to treat penetrating wounds conservatively, watching the case carefully for the first three or four days for hemorrhage and infection and not hesitating on early indications for radical measures. I believe the withdrawal of fluid from the chest and the replacement of air to be a great advantage in the conservative treatment in such cases.

DR. C. M. VAN ALLEN, New Haven, Conn.: On the subject of coagulation of the blood that is accumulating in the chest in these cases, I should like to ask Dr. Allen if he has any explanation for the failure of coagulation of the blood as it lies in the pleura. I should like to add an observation of my own in that regard.

Some time before the present meeting, a patient was admitted to the hospital who had shot himself with a revolver in the left side of the chest. On admission, he showed a large hemothorax. Expectant treatment was used, and two weeks later he seemed to be fully recovered except that he had a large mass of blood in the pleural cavity. We undertook aspiration of the blood. The blood flowed through the needle easily, and we took out about 1,000 cc. the first time, stopping simply because we felt that we ought not to take out more than that at one time. The blood was still fluid at the end of two weeks. When it went into the bottle, it clotted within a minute or so, so that on being shaken, it was completely jellied.

In this case the blood that stayed in the chest for two weeks clotted immediately on being eliminated from the chest, and apparently in that case, at least, we would have been misled if we had taken the clotting as a sign of fresh bleeding.

DR. ALLEN: In the consideration of this series of cases, I did not mention the treatment for larger wounds of the chest wall and lung, as there were none of that type. Duval and others advocated thorough exploration of the chest, repair of the lung, and removal of the large missiles in this type of case. In cases with bullet wounds that produced small wounds of the chest wall and lungs, it was not found necessary to explore. This distinction is important.

I agree with Dr. Lilienthal that one should not attempt to aspirate the hemothorax immediately after it has formed. It seems logical to suppose that aspiration of the hemothorax at this time would increase the hemorrhage from the wound in the lung. I have been unable to find definite proof, however, that gradual aspiration of the blood would increase the hemorrhage. I think that one may safely turn the patient so that the closed wound is dependent and thus allow the hemothorax to leak out slowly.

In regard to the failure of the blood to clot within the pleural cavity, Henry and Elliot in a series of cases during the war determined that the blood con-

tained in a hemothorax was really defibrinated blood. An exudate from the pleura often contaminated the blood and produced the clotting when all the fluid was withdrawn from the pleural cavity. They stated that the blood contains no fibrinogen. This does not seem to me to hold in all cases. In certain cases observed during the war all the blood contained within the pleural cavity was found to be liquid, and there were no masses of fibrin. I do not know how to explain this on the basis of immediate clotting and subsequent defibrination.

Dr. P. N. Coryllos, New York: The penetrating wounds of the thoracic cavity due to small bullets should be distingished from the large openings of the thoracic cavity caused by a bayonet, a knife, fragments of shells or trench torpedoes, as were those seen during the World World. In these cases, because of the wide opening of the pleural cavity and the collapse of one lung, asphyxia was (in the absence of great hemorrhage) the most immediate danger. Survival or immediate death depended on the resistance offered by the mediastinum. An elastic and yielding mediastinum that allowed serious interference with function of the other lung was incompatible with the survival of the wounded. However, during my service in Verdun, France, I saw a number of cases of unbelievably wide openings of the chest in which I consider that the survival during transportation from the battlefield to the advance ambulance was due to the obduration of the wound by the clothes of the wounded or to the tight dressing applied to the wound. In these cases the only thing to do was to trim the wound rapidly, to stop the hemorrhage by tying the bleeding points, even if it were on the lung tissue, and to close the cavity. The after-treatment depended on the behavior of the wound. Generally no evacuation of the fluid accumulating in the thoracic cavity was done before the third or fourth day, unless vitally indicated. After that time, since, as a rule, infection would set in, the fluid was tapped and as much as possible gradually aspirated. In these cases the infections were usually anaerobic. If the patient survived the first three to five days, empyema generally set in, the management of which was easer than that of anaerobic infection. Besides these cases, however, I saw, some marvelous recoveries with practically primary healing.

Another class of wounds that I should like to mention were wounds of the lung caused by small splinters of shell or trench torpedoes that exploded a short distance from the patient and therefore possessed great momentum. In these wounds no pneumothorax or even hemothorax of any importance was present. They appeared to be slight injuries. Two or three days later, however, symptoms of pneumonitis would develop on the affected side, and the patient would soon die with signs of severe general toxemia. Postmortem examination would disclose signs of deep disorganization of the affected parenchyma and gas gangrene rapidly spreading around a foreign body that sometimes did not exceed the size of a small pea or lentil.

I mention these cases because they show the extreme variability of the different penetrating wounds of the thoracic cavity and because of the possibility of standardized therapeutic methods for them. I firmly believe that in the second variety of cases, after the localization of the foreign body, the best method is to perform a thoracotomy and trim out the wounded lung parenchyma, in other words, to apply to the lung the same principles of preventive débridement that gave such brilliant results in the treatment for wounds of the knee joints and of the soft tissue.

On the other hand, I should be extremely conservative in the treatment of bullet wounds, although I agree with Dr. Allen that the early evacuation of

hemothorax, made with caution, is an excellent measure. It often prevents the development of secondary infection and hastens recovery.

DR. HOWARD LILIENTHAL, New York: I have had some experience with gunshot wounds of the chest and other wounds, too. There are some things that Dr. Allen has said with which I cannot quite agree. I do agree with Dr. Allen if he is sure of the kind of injury that the patient has had, but this is very difficult. A patient may die of hemorrhage from an intercostal artery that has been wounded. Nonintervention in such a case would be serious, resulting in death from hemorrhage into the chest. Or there may be fatal bleeding outside which, in the cases such as those illustrated by Dr. Allen, might, of course, be mistaken for intrathoracic bleeding with external leakage. The presence of clot in the recently exuded blood is a very important sign and calls for immediate intervention.

Was the precentage of hemoglobin 60 immediately after the hemorrhage?

DR. DUFF ALLEN: The next day.

DR. HOWARD LILIENTHAL: That is perfectly possible; but I could not conceive of a hemoglobin reading of 60 per cent immediately after the hemorrhage. The hemoglobin reading should then be just what it was before the man was injured.

Blood pressure readings are of the greatest importance in these cases in deciding on operation.

I do not think that hemothorax should be aspirated, because the intrapleural tension tends to hold the lung in compression and maintain closure of the wound in the lung if there is one. On aspiration the lung is expanded, the pulmonary wound reopens, and the hemorrhage begins again. I should rather use artificial pneumothorax than aspiration in cases of this kind.

ETIOLOGY OF PRIMARY BRONCHIECTASIS*

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For the purposes of this paper bronchiectasis is considered primary when the ulceration and dilatation of the bronchial tree cannot be ascribed to any preceding or underlying pathologic process in the lungs or bronchi. Thus I have excluded from consideration all lesions occurring in the course of tuberculosis: both the true tuberculous ulcerations of the bronchial wall and the more common forms of bronchial dilatation seen in chronic fibroid phthisis, in lungs collapsed by artificial pneumothorax or by thoracoplasty, and in old atelectatic lungs. The latter lesions are usually mere mechanical dilatations due to the stretching and distortion of the bronchi by fibrous tissue, and, on section, the bronchial wall is seen to be intact, in contrast to primary bronchiectasis in which ulceration and destruction of the elastic tissue are conspicuous. The definition also excludes bronchiectasis secondary to stricture of the bronchus due to aneurysm, neoplasm or foreign body, as well as dilatations caused by fibrous contractions in pleurisy, cirrhosis of the lung and unresolved pneumonia. I shall disregard the relatively rare cases of congenital cystic bronchiectasis first described by Grawitz[1] and the more common acute dilatations of the bronchioles following infection with *B. influenzae*. This leaves for consideration as primary or essential bronchiectasis only those cases of nontuberculous ulceration and dilatations of the larger bronchi characterized by a chronic course, distressing cough, and large amounts of sputum which may be very foul.

Primary bronchiectasis is analogous to aneurysm in many respects.[2] Both arteries and bronchi are hollow muscular tubes, the main strength of which is derived from the dense sheet of elastic tissue in their walls.[3] Arteries cannot dilate until the integrity of the elastic tissue layer is destroyed by the action of *Spirochaeta pallida* permitting the formation of sacculated, cylindric or fusiform aneurysms. Similarly,

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*From the New York State Hospital for Incipient Tuberculosis.

1. Grawitz, P.: Ueber angeborne Bronchiectasie, Virchows Arch. f. path. Anat. **82**:217, 1880.

2. This similarity between aneurysm and bronchiectasis was suggested to me by Dr. H. A. Bray, Superintendent of the New York State Hospital for Incipient Tuberculosis.

3. Macklin, C. C.: Functional Aspects of Bronchial Muscle and Elastic Tissue, Arch. Surg. **19**:1212 (Dec.) 1929.

in my opinion, the bronchi present the sacculated, cylindric or fusiform dilatations characteristic of primary bronchiectasis only after the elastic tissue fibers have been weakened and ruptured by the action of an anaerobic group of organisms which includes among its members *Treponema microdentium* and *Treponema macrodentium*.

In previous contributions,[4] I have shown that Vincent's angina, pulmonary gangrene and pulmonary abscess are all due to the symbiotic action of the group of anaerobes found in pyorrhea alveolaris; this group includes *T. microdentium, T. macrodentium, S. Vincenti, S. buccalis,* fusiform bacilli, vibrios and cocci. In this paper I propose to present clinical and experimental evidence to show that the essential lesion of primary bronchiectasis, i. e., the destruction of the elastic coat of the bronchus, is caused by focal necrosis due to infection with this same fusospirochetal group of anaerobic organisms. These organisms are constantly present in the sputum of active cases of bronchiectasis and can be demonstrated in properly stained sections deep in the tissues of the diseased bronchi. With these anaerobic organisms bronchial disease may be produced in rabbits which is comparable to bronchiectasis in man.

Many observers have noted the presence of spirochetes and other organisms of the mouth in the sputum from cases of bronchiectasis (Leyden and Jaffe,[5] Rona,[6] Buday,[7] Nolf,[8] Pilot and Davis,[9] Kline and Berger [10] and Smith 11).

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4. Smith, D. T.: Experimental Aspiratory Abscess, Arch. Surg. **14**:231 (Jan.) 1927; Bronchopulmonary Spirochetosis, Am. Rev. Tuberc. **15**:352, 1927; Fusospirochetal Disease of the Lungs, ibid. **16**:584, 1927; Fusospirochetal Diseases of the Lungs, Tubercle **9**:420, 1928; Relation of Vincent's Angina to Fusospirochetal Diseases of the Lungs, J. A. M. A. **94**:23 (Jan. 4) 1930; Fusospirochetal Disease of the Lungs Produced with Cultures from Vincent's Angina, J. Infect. Dis. **46**:303 (April) 1930.

5. Leyden and Jaffe: Ueber putride (fötide) sputa nebst einigen Bemerkungen über Lungenbrand und putride Bronchitis, Deutsches Arch. f. klin. Med. **2**:488, 1867.

6. Rona: Zur Aetiologie und Pathogenese der Plaut-Vincentschen angina, Arch. f. Dermat. u. Syph. **74**:171, 1905.

7. Buday: Histologische Untersuchungen über die Entstehungsweise der Lungengangrän, Beitr. z. path. Anat. u. z. allg. Path. **48**:70, 1910.

8. Nolf, P.: Fetid Spirillar Bronchitis and Pulmonary Gangrene, Arch. Int. Med. **25**:429 (April) 1920.

9. Pilot, I., and Davis, D. J.: Studies in Fusiform Bacilli and Spirochetes; Their Rôle in Pulmonary Abscess, Gangrene and Bronchiectasis, Arch. Int. Med. **34**:313 (Sept.) 1924.

10. Kline, B. S., and Berger, S. S.: Spirochetal Pulmonary Gangrene Treated with Arsphenamins, J. A. M. A. **85**:1452 (Nov. 7) 1925.

11. Smith, D. T. (footnote 4, references 1, 2 and 3).

In demonstrating the spirochetes and fusiform bacilli in the sputum from cases of bronchiectasis, special care in the selection of the specimen for examination is important. The residual sputum from the depth of the lungs is the most desirable, so I try to obtain the last purulent material that is raised after a coughing spell in the morning, or better still, the last material raised following postural drainage. In many cases the residual sputum will contain spirochetes and fusiform bacilli when chance specimens taken during the day or even the first portion raised during postural drainage fails to show these anaerobic

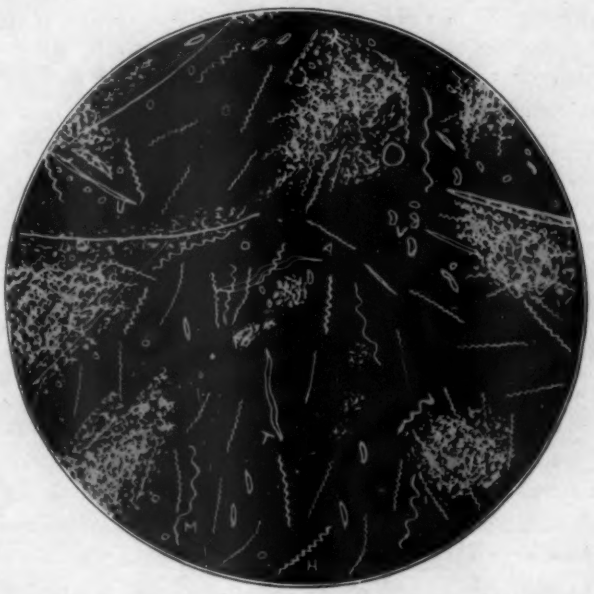

Fig. 1.—Drawing made from a dark-field preparation of a granule from the sputum of a patient with chronic bronchiectasis. *A* indicates T. microdentium; *H*, T. macrodentium; *M*, S. Vincenti; *T*, S. buccalis; *U*, large fusiform bacillus; *V*, vibrio.

organisms. In other cases, spirochetes and fusiform bacilli are found in the sputum only when the patient is having an increase in symptoms. The fusiform bacilli are best stained by either Sterling's gentian-violet or carbol-gentian-violet. The thicker spirochetes, *S. buccalis* and *S. Vincenti,* may also be seen with the gentian-violet stain, but the smaller spirochetes, *T. macrodentium* and *T. microdentium,* are generally not stained by this method. They have to be studied by either the Fontana stain or preferably the dark-field apparatus (fig. 1). Smears for the Fontana stain and wet preparations for dark-field

examination have to be made exceedingly thin, otherwise the delicate spirochetes are all hidden by débris.

During the past five years I have had the opportunity of studying 100 cases of nontuberculous bronchial disease. Bronchiectasis was demonstrated in 60 cases by the injection of iodized poppy seed oil 40 per cent. Spirochetes, fusiform bacilli, vibrios and cocci were found in 49 or 82 per cent, and in every one of the 49 cases, the iodized oil revealed the characteristic picture of bronchiectasis. Among the 51 cases in which spirochetes and fusiform bacilli were not found in the sputum, 40 showed essentially normal bronchi by the injection of iodized oil, while 11 had dilated bronchi. The bronchial disease in the latter group might have been caused by some other type of organism or the characteristic anaerobes might have disappeared before the sputum was examined. A spontaneous cure accounts for 3 of these 11 cases since at the time of the injection of iodized oil there was no cough or expectoration, although there was a history of

Correlation of Bacteriology and Iodized Oil

Iodized poppy seed oil 40% in 100 cases of bronchial disease	60+	49	Spirochetes and fusiform bacilli
		11	No spirochetes or fusiform bacilli
	40—		No spirochetes or fusiform bacilli

foul sputum present over a period of years. In two other cases I have observed the spontaneous disappearance of the fusospirochetal organisms when the patients were treated by postural drainage. In a number of patients treated with both postural drainage and repeated courses of neoarsphenamine or sulpharsphenamine the spirochetes disappeared first, the fusiform bacilli and the vibrios next, and the cocci last. Indeed, the cocci often persist for years after the other organisms are gone and after the patient is in excellent physical condition.

Bronchiectasis may begin in any one of three ways. A membranous exudate may form on the surface of the bronchial wall similar to the membrane of Vincent's angina, and ulceration take place beneath this covering. Chevalier Jackson studied two such cases with the bronchoscope.[12] More commonly bronchopneumonia is produced by the anaerobic organisms in which certain of the terminal bronchi are filled solidly with exudate. These organisms then invade the bronchial wall, destroying the elastic tissue support and produce bronchiectasis. In the third type, bronchiectasis develops in the bronchi in which a

12. Jackson, C.: Ulcerative Bronchitis Due to Vincent's Organisms, J. A. M. A. **83**:1845 (Dec. 6) 1924.

lung abscess is draining. The constant contact of the fusospirochetal material with the bronchus finally results in infection and ulceration. This process is illustrated in figure 2. Some of the bronchial mucosa cells still show cilia, but the spirochetes followed by fusiform bacilli, vibrios and cocci have penetrated deeply into the bronchial wall. To the left of the area illustrated, the bronchial mucosa was already destroyed, and the organisms were penetrating the elastic tissue layer.

The next stage in the process of bronchial ulceration is shown in figures 3 and 4. Here a bronchial lesion hardly larger than the head of a pin has already cut entirely through and destroyed the integrity

Fig. 2.—Drawing made from the bronchus of a child with a pulmonary abscess. The sputum from the abscess drained through this bronchus. Fusiform bacilli and spirochetes are seen invading the wall of the bronchus. Levaditi stain.

of the elastic tissue layer. The size, distribution and location of the lesions determine whether the resulting dilatation is fusiform, cylindric or sacculated (Fig. 5).

Sections from twelve cases of bronchiectasis have been examined for fusiform bacilli and spirochetes. The tissues were stained by the method introduced by Levaditi for the demonstration of *Spirochaeta pallida*. Spirochetes and fusiform bacilli were found in eight of twelve cases. The ones that did not show the organisms were old chronic cases of years' duration. Dr. Leroy U. Gardner of the Saranac Lake Laboratory gave me the opportunity to examine sections from

six other cases which were stained with Goodpasture stain following fixation in Zenker's solution. Spirochetes cannot be demonstrated by this method, but fusiform bacilli were found in four of the six cases. Buday [7] and Pilot, Davis and Shapiro [13] have also demonstrated spirochetes and fusiform bacilli in the bronchial wall tissue from cases of bronchiectasis.

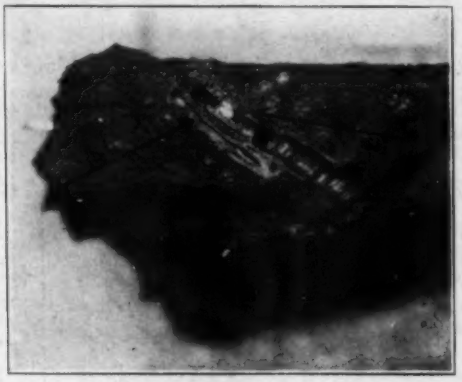

Fig. 3.—Photograph of a small bronchial ulcer. Smears from the lesion showed spirochetes, fusiform bacilli and cocci.

Fig. 4.—Photomicrograph of a section of the bronchial ulcer shown in figure 3. The mucosa can be seen covering a portion of the surface. The elastic tissue and muscular layers are completely destroyed in the central portion; × 150.

EXPERIMENTS

In a previous study of experimental pulmonary disease in guinea-pigs caused by aspiration of fusospirochetal material, I observed ulcera-

13. Pilot, I.; Davis, D. J., and Shapiro, I. J.: Studies of Fusiform Bacilli and Spirochetes, Am. Rev. Tuberc. **8**:249, 1923.

tions of the bronchi which were not of sufficient extent to be called bronchiectasis.[14] Allen [15] and Harkavy [16] observed similar lesions in the smaller bronchi of dogs infected with fusospirochetal material. Weidlein and Herrmann [17] obtained definite ulceration and dilatation of the bronchial wall in one dog by fastening cotton soaked with fusospirochetal material in the bronchi.

In the following experiments I attempted to produce bronchiectasis in rabbits by the simple aspiration method, since the clinical data suggest that this is the route by which the anaerobic organisms from pyorrhea alveolaris reach the bronchi. Material from three different sources was used. In the first experiment, scrapings from about the

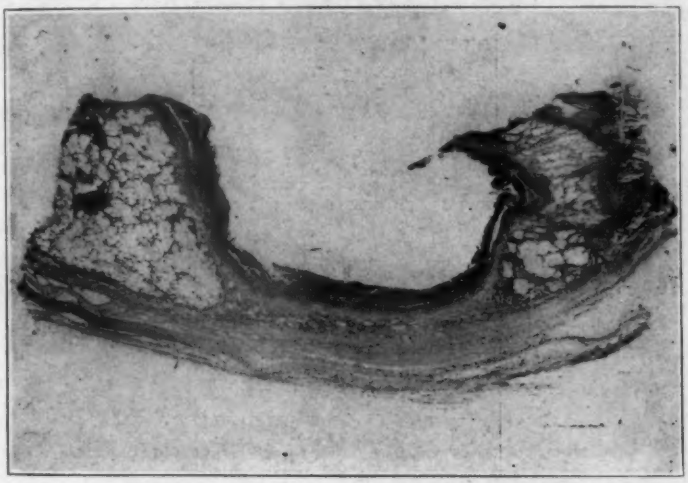

Fig. 5.—Photomicrograph of a section from an old case of bronchiectasis. The elastic tissue and muscular layers are largely destroyed and are surrounded by a dense layer of fibrous tissue; × 10.

teeth of patients with moderately severe pyorrhea was employed. For the second experiment, sputum from a case of acute fusospirochetal bronchitis was used. Sputum from a case of pulmonary abscess was utilized in the third experiment. In the fourth experiment control inoculations were made with pure cultures of: (1) *Staphylococcus*

14. Smith, D. T. (footnote 4, reference 1).

15. Allen, D. S.: Etiology of Abscess of the Lung, Arch. Surg. **16**:179 (Jan.) 1928.

16. Harkavy, J.: The Pathogenesis of Aspiratory Abscess of the Lung, Arch. Int. Med. **43**:767 (June) 1929.

17. Weidlein, I. F., and Herrmann, L. G.: Abscess of the Lung: Experimental Study in Chronicity, J. A. M. A. **91**:850 (Sept. 22) 1928.

aureus, (2) aerobic hemolytic streptococci, (3) anaerobic hemolytic streptococci, (4) green-producing streptococci, (5) an anaerobic streptothrix, (6) Friedländer's bacillus and (7) influenza bacillus. All of these organisms were isolated from the sputum of cases of nontuberculous pulmonary disease.

Experiment 1.—A guinea-pig was inoculated in the groin with 0.5 cc. of pyorrhea material. After eight days the animal developed a large abscess containing thin foul-smelling purulent material which showed on examination large numbers of spirochetes, fusiform bacilli, vibrios and cocci. One-fourth cubic centimeter of this material was introduced into the trachea of each of six rabbits. The rabbits were anesthetized, the trachea dissected out and elevated to the surface, a 14 gage needle introduced into the trachea, and the material was slowly introduced with a tuberculin syringe. The head of the animal was elevated and the

Fig. 6.—Roentgenogram of the chest of a rabbit. The lungs show a sacculated dilatation by iodized oil.

body rotated so that the purulent material would flow into the left lower lobe. Four days later roentgenograms of the rabbits were made, and all were found to have a shadow in the lower part of the left lung. The same day a dose of (15 mg. per kilogram) sulpharsphenamine was injected intravenously. The sulpharsphenamine was given with the idea that some of the spirochetes would be killed, and the progress of the disease retarded, so that the ulceration might be confined to the bronchi rather than invade the whole lung as in abscess or gangrene.

One animal died on the fifth day with extensive gangrene of the left lung. One died on the sixth and two on the eighth day with abscess of the left lung complicated by empyema. One rabbit, which lived for fifteen days, on postmortem injection of iodized oil presented the picture of bronchiectasis (fig. 6). At necropsy, there were extensive ulceration and destruction of the bronchial wall, and the characteristic fusospirochetal combination of organisms were demonstrated in smears made from the lesion. The sixth rabbit made a complete recovery.

Experiment 2.—A guinea-pig was inoculated in the groin with sputum from a case of acute bloody bronchitis, which contained large numbers of spirochetes, fusiform bacilli, vibrios and cocci. An abscess appeared in six days, and pus from this, in amounts of 0.25 cc. was injected into the trachea of six rabbits as in experiment 1. Roentgenograms showed shadows in the left lung of all the animals on the fourth day when they were given sulpharsphenamine intravenously (15 mg. per kilogram). A second dose of sulpharsphenamine was given two days later.

Two rabbits died on the seventh day with pulmonary gangrene; one died on the ninth day and one on the twelfth day with abscess and empyema. The last two rabbits died on the sixteenth and twentieth days, respectively, and bronchiectasis was demonstrated by both postmortem injection of iodized oil and

Fig. 7.—Photomicrograph of multiple dilatations of the bronchi of a rabbit infected with fusospirochetal material; × 10.

necropsy (fig. 7). Fusiform bacilli, vibrios and cocci were found in smears from the lesions, but no spirochetes. The spirochetes were probably killed by the arsenic therapy.

Experiment 3.—In this experiment, an attempt was made to increase the resistance of the rabbit by intravenous injections of heat-killed abscess material. Sputum, containing spirochetes, fusiform bacilli, vibrios and cocci from a case of pulmonary abscess was injected into the groin of a guinea-pig. Some of the purulent material from the experimental abscess was heated in a water bath of 60 C. for one hour, and then cultivated anaerobically to demonstrate the sterility. Ten rabbits received in the ear vein 0.25 cc. of this material in 1 cc. of saline solution. A second and third injection were given at weekly intervals. A week after the last injection, 0.25 cc. of the living fusospirochetal material, which had been kept alive by transfer from pig to pig at eight to ten day intervals, was

introduced into the trachea as in experiment 1. Roentgenograms of the chest, made four days later, showed some evidence of disease in eight of the ten animals. Either the infecting organisms had lost some of their virulence, or the rabbits had acquired a considerable degree of resistance, for the animals all recovered within two weeks.

The ten rabbits were then reinoculated intratracheally with 0.5 cc. of fusospirochetal material. On the fourth day after inoculation, roentgenograms of all the animals showed extensive infection of the left lung. On the same day, each rabbit was given a dose of sulpharsphenamine intravenously (15 mg. per kilogram). Two rabbits died of pulmonary gangrene on the fifth day and two others on the sixth day. The survivors were given another dose of sulpharsphenamine on the sixth day. Three other animals died of pulmonary abscess between the eighth and tenth days of the experiment.

The shadows in the surviving rabbits gradually cleared over a period of two months, as demonstrated by the roentgenograms. One animal recovered entirely. The other two presented bronchiectasis which could be demonstrated in the living rabbit with injection of iodized oil. The animals were killed, and the diagnosis confirmed at necropsy.

Experiment 4.—As a control to the foregoing experiments each of two rabbits received intratracheally: a saline suspension of one fourth of the total growth of a pure culture of *Staphylococcus aureus* from a blood agar slant; the total growth from two blood agar slants of a pure culture of an aerobic hemolytic streptococcus; the total growth from two blood agar slants of a pure culture of an anaerobic hemolytic streptococcus; the total growth from two blood agar slants of a pure culture of a green-producing streptococcus; total growth from a blood agar slant of a streptothrix, and the total growth from two blood agar slants of a pure culture of *B. influenzae*. Five rabbits received intratracheally one fourth of the contents of a blood agar slant of a pure culture of a Friedänder's bacillus.

On the fourth day, all seventeen animals showed evidence of disease in the roentgenograms, but with the exception of three of the five that received the Friedländer's bacillus, all the rabbits had normal lungs at necropsy three weeks later. No permanent damage was produced in the bronchi by any of these seven types of organisms.

COMMENT

The influenza bacillus is present in a certain percentage of cases of bronchiectasis, and some authorities assume that it is the essential cause of the disease. During the last great epidemic, Opie, Freeman, Blake, Small and Rivers,[18] found influenza bacilli producing purulent bronchiectasis of the terminal bronchi in patients dying of postinfluenzal pneumonia. Later Blake and Cecil[19] demonstrated similar lesions in monkeys that had been infected with pure cultures of *B. influenzae*. It has, however, never been conclusively proved that *B. influenzae* can destroy the elastic tissue of the larger bronchi. Although

18. Opie, E. L.; Freeman, A. W.; Blake, F. G.; Small, J. C., and Rivers, T. M.: Pneumonia Following Influenza, J. A. M. A. **72**:556 (Feb. 22) 1919.

19. Blake, F. G., and Cecil, R. L.: Nine Studies on Experimental Pneumonia, J. Exper. Med. **32**:691, 1920.

the work of Garvin, Lyall and Morita [20] shows that this organism can produce a chronic bronchitis with moderate dilatations of the bronchioles, I am not convinced that the influenza bacillus can initiate the type of bronchiectasis discussed in this paper.

On the basis of etiology, there is no sharp line of differentiation between pulmonary gangrene, pulmonary abscess and bronchiectasis. My experience confirms the opinion of Whittemore [21] that every case of bronchiectasis presents more or less involvement of the parenchyma. Exactly the same combination of anaerobic organisms that appears to be the cause of pyorrhea alveolaris is found in pulmonary gangrene, pulmonary abscess and bronchiectasis. In the first experiment recorded, material from pyorrhea alveolaris was used; in the second, sputum from a case of fusospirochetal bronchitis; and in the third, sputum from a case of pulmonary abscess. The same combination of anaerobic organisms was present in the material from the three sources and it was found that some rabbits in each group developed gangrene, some abscess and some bronchiectasis.

SUMMARY AND CONCLUSION

The essential lesion in primary bronchiectasis is a focal necrosis of the elastic tissue in the bronchial wall due to infection with the fusospirochetal group of anaerobic organisms. This fusospirochetal group, comprising *T. macrodentium, T. microdentium, S. Vincenti, S. buccalis,* fusiform bacilli, vibrios and cocci, are the same organisms that are found in pyorrhea alveolaris, Vincent's angina, pulmonary abscess and pulmonary gangrene.

These organisms have been seen in the sputum of forty-nine of sixty patients proved to have bronchiectasis by the iodized oil test.

Spirochetes and fusiform bacilli were found in sections of bronchial dilatations after staining by Levaditi's method in eight of twelve cases which came to necropsy. Fusiform bacilli were demonstrated in pathologic sections from four of an additional six cases of bronchiectasis after staining by Goodpasture's method.

In animal experiments, fusospirochetal material from varied sources (pyorrhea alveolaris, fusospirochetal bronchitis and pulmonary abscess) caused bronchiectasis as well as pulmonary abscess and pulmonary gangrene in rabbits.

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20. Garvin, A. H.; Lyall, H. W., and Morita, M.: Chronic Nontuberculous Lung Infection, Am. Rev. Tuberc. **1**:16, 1917.

21. Whittemore, W.: The Treatment of Chronic Broncho-Pulmonary Suppurative Lesions Limited to One Lobe of the Lung, New England J. Med. **199**: 1213, 1928.

Control inoculations with pure cultures of (1) *Staphylococcus aureus,* (2) aerobic hemolytic streptococci, (3) anaerobic hemolytic streptococci, (4) green-producing streptococci, (5) anaerobic streptothrix, (6) Friedländer's bacilli and (7) influenza bacilli failed to produce damage to the bronchi.

The fusospirochetal group of organisms is probably the cause of primary bronchiectasis.

ABSTRACT OF DISCUSSION

Dr. F. T. Lord, Boston: Much credit is due Dr. Smith for his painstaking work in this difficult bacteriologic field. In both the postoperative group of patients with abscess of the lung and the group on which operation had not been performed, the disease arises so frequently apart from lobar or obvious bronchopneumonia as to suggest that it is not an accident of resolution but an independent condition. Ingress into the deeper parts of the respiratory tract of infected material from above is to be regarded as the chief cause of pulmonary abscess. It is largely as a result of Dr. Smith's investigations that increasing attention has been paid to spirochetes and fusiform bacilli as a cause of abscess of the lung. As he has pointed out, the bacterial flora of abscess is that of the tonsillar crypts and the teeth, and the same assortment of organisms, including spirochetes, fusiform bacilli, cocci and vibrios, obtains in postoperative and nonoperative abscess. Animal experiments suggest that not one organism alone is the cause, but that symbiosis is essential for the production of abscess. Bacterial association favorable to the multiplication of certain organisms in culture mediums has long been noted and may be necessary for the production of pulmonary abscess, but the necessity for the introduction of this principle and the inability to establish the presence of these organisms in all cases of abscess make it inadvisable to accept without question their etiologic relation with the disease. It may nevertheless be said that from his work certain cases of abscess and bronchiectasis are known probably to be due to these organisms.

Bronchiectasis, from a pathologic point of view, is uncommon and only rarely merits an independent position. It usually arises under conditions that make it desirable to regard it as a relatively unimportant complication in the course of a bronchopulmonary disturbance. The pathologic process in the lung is ordinarily much more important than the bronchial dilatation. Roentgenologic interpretations are largely responsible for the frequency and undue importance accorded this condition clinically, and it seems unfortunate that the term is so freely used.

Dr. Carl A. Hedblom, Chicago: I was particularly interested in Dr. Smith's paper because of the light it throws on the etiology of bronchiectasis. From clinical studies we recognize a variety of causes for this condition, the most important of which are the acute infectious diseases of childhood, bronchopneumonia occurring at any age and the various conditions that result in permanent atelectasis and those that produce an extensive fibrosis of the lung, including fiboid phthisis. In a considerable proportion of cases the cause cannot be determined. A considerable proportion of these cases of indeterminate etiology are probably congenital. Sauerbruch has expressed the opinion that most of the cases of leftsided involvement are congenital. I am inclined to the opinion that aspiration of such organisms as Dr. Smith described may be the determining factor in a large proportion of the cases of indeterminate etiology.

With regard to pathologic changes, I cannot quite agree with my good friend, Dr. Lord. Necropsy in cases of long duration and in patients who died of complications would naturally be expected to show pulmonary involvement in large proportion. We see many patients, however, who presumably have had bronchiectasis for many years, who have no outstanding symptoms except cough and sputum and who remain in fairly good health. Physical examination shows only a few râles, and roentgenograms show little or no evidence of pathologic processes in the parenchyma of the lung. Pathologists usually do not see these cases until complications have developed.

One of the practical conclusions that we may draw from Dr. Smith's investigation is the importance of preoperative prophylaxis of the mouth and throat and of treatment with arsphenamine in cases in which we have reason to believe that spirochetes are among the infective organisms.

Dr. C. M. Van Allen, New Haven, Conn.: Dr. Smith is to be congratulated on his work, because, beginning with his paper presented two or three years ago before the Society, it represents the main work that has fixed this spirochetal disease as one of the main factors in chronic suppurative diseases of the lung. Following that paper his work has been corroborated, of course, by Hedblom and many others in every respect that he indicated.

There is one point in which I do not quite agree with his conclusions, and that is merely an academic issue, a question of terminology. I object to calling spirochetal disease the cause, the etiology, of chronic abscess of the lung and of bronchiectasis just because it happens to be found in a high percentage of cases. I am sure that Dr. Smith would not say, for instance, just because he found 60, 70, 80 or 90 per cent of all tonsils chronically diseased infected with spirochetes that spirochetes were the cause of tonsillitis. I think the stand to take is that the spirochetal disease is a secondary contaminant and that it is responsible for the disease, that is, for the chronic stages of the disease.

Dr. Hedblom has pointed out that in most cases there is probably a lesion in the bronchial tree to start with, a locus minoris resistentiae, so to speak, on which the organisms can implant themselves and proceed to destroy the bronchial tree still further to cause the exacerbations. We pointed out that they appear in the exacerbations.

He has chosen a rather unfortunate animal for his experimental work, because the rabbit is very susceptible to spirochetal disease. In the rabbit the introduction of spirochetes is quickly followed by necrosis and destruction of the tissues. The dog represents a different picture. In the dog it is difficult to produce a bronchiectasis or an abscess, a chronic lesion, of the virgin lung by means of spirochetes. We have been able to produce chronic lesions with the spirochetes in the dog, but only after we have produced a locus minoris resistentiae, an acute abscess, or some other lesion, by burning the bronchus beforehand and then implanting the organisms on that lesion. I think that that is the main issue. The bacteria form a very important part of the disease, but they represent a secondary contamination and are the means by which the diseases are mainly propagated.

Dr. David T. Smith, Ray Brook, N. Y.: The point Dr. Lord brought up is a pertinent one and I think I can illustrate what I wish to say much better than I can describe it. I have been engaged for four years in an attempt to isolate all the organisms involved in abscess of the lung and bronchiectasis and to recombine them so as to determine the combination necessary to reproduce the disease.

The slide shown is an illustration of a culture of *T. macrodentium.* I have also isolated a few strains of the larger *T. macrodentium.* These organisms in pure culture are absolutely harmless to animals.

The next slide is that of a pure culture of the large fusiform bacillus. I have isolated a number of strains of this and several small forms of fusiform bacilli.

I have isolated several cultures of the vibrio. In one culture I must have had something wrong with the salt content of the medium, for all the flagelli became hypertrophied to such an extent that they could be seen readily with the dark-field apparatus.

I found a number of different kinds of cocci in these cases of abscess and bronchiectasis. The cocci produce simple pyogenic lesions when introduced into animals.

The various combinations of these organisms were tested. Neither spirochetes nor fusiform bacilli alone produced disease. The combination of the two likewise failed to produce disease. With the anaerobic hemolytic streptococcus, a little pus developed in the groin of a guinea-pig, but no necrosis and no foul odor. When the vibrio was added to the streptococcus, a much more extensive lesion was obtained, but still no necrosis and no odor. The addition of the fusiform bacillus to the coccus and the vibrio resulted in a small amount of necrosis, but no odor. The addition of the spirochetes to the coccus, vibrio and fusiform bacillus gave a severe lesion with extensive necrosis and foul odor. The resulting disease could then be transferred from pig to pig almost indefinitely.

That, of course, brings up the question which is in everybody's mind as to whether these spirochetes are secondary invaders. The spirochete is not secondary to the others. It is a concomitant rather than a secondary infection, that is, the spirochetes and fusiforms, vibrios and cocci all go down together into the lungs. Aspiration of the cocci alone results in a simple pyogenic infection of the lungs.

As Dr. Hedblom has pointed out, bronchiectasis does at times follow (1) acute infections of childhood, (2) pneumonia and (3) aspiration of foreign bodies. But bronchiectasis is not a constant sequela in these conditions, so it is more logical to suppose that only those patients develop bronchiectasis who are so unfortunate as to aspirate some of the anaerobic organisms from the mouth during the course of the disease. Congenital bronchiectasis, of course, is a possibility, but I fear that I cannot agree with Sauerbruch that it is a common observation, since it is encountered rarely in routine necropsies on infants. I am afraid Sauerbruch has not distinguished clearly between congenital bronchiectasis and bronchiectasis beginning in early childhood as an infectious process.

I heartily agree with the two points mentioned by Dr. Hedblom in regard to treatment. If this work means anything at all, it means that the organisms present in pyorrhea have something to do with bronchiectasis, abscess of the lung and gangrene. The best method of preventing them is to prevent these organisms getting into the lung. Personally, I feel that arsenic therapy is of some value in all cases of bronchiectasis and of great value in certain cases. In the last five years, we have found a number of cases, some of which are still under observation, in which excellent results were obtained by postural drainage and arsenic therapy. The patients were given postural drainage for from three to six months before treating them with arsenic, so that those who were going to get well by posture drainage alone could be eliminated. Then arsenic therapy was added and a number made a spectacular recovery.

I am glad Dr. Van Allen brought up the question of the relative susceptibility of the rabbit and the dog to these organisms. It is true that the rabbit is more

susceptible than the dog, but man also is very susceptible, and in this respect may be more like the rabbit than the dog. On the other hand, the dog is not completely resistant since abscesses have been produced in dogs with these organisms by Dr. Van Allen himself, by Duff Allen, Crowe and Scharff, Johannides and Hedblom, Harkevy, and Widelein and Schleuter.

Atelectasis is a factor in the development of certain cases of abscess and bronchiectasis, as Dr. Coryllos has pointed out. These are anaerobic organisms and do not readily survive on the surface of the bronchus, that is, they cannot live on the surface of a bronchus as a streptococcus or an influenza bacillus can. They either disappear completely and leave no disease or they invade deeply into the bronchial wall, where they destroy the elastic tissue and produce a bronchiectasis.

CHANGES IN THE PULMONARY CIRCULATION INDUCED BY EXPERIMENTALLY PRODUCED ARTERIO-VENOUS FISTULA

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The altered hemodynamics of the pulmonary circulation in response to an increase in the volume flow of blood have been subjected to experimental observation through several different methods. The most direct studies have been made with a Starling heart-lung preparation [1] or a modification thereof.[2] In these preparations the lung is a surviving organ isolated from any possible control by the central nervous system, and deductions as to the state of affairs in the intact organism are to be drawn with caution. Ligation of one branch of the pulmonary artery has been employed as a device to increase the volume flow in the contralateral lung,[3] but this method also has its obvious limitations. Wiggers [4] augmented the venous return to the heart by the intravenous injection of saline solution, again a method that is at variance with normal physiologic occurrences.

In the experiments herewith reported the venous return to the heart and consequently the volume flow of blood through the lungs have been increased experimentally by the opening of an arteriovenous fistula inserted in the systemic circuit. This procedure has been carried out on normally breathing cats and closely simulates, as far as volume flow is concerned, what happens when a previously resting person undertakes moderate exercise. In contrast to what occurs in exercise, it may be pointed out that the establishment of an arteriovenous fistula entails a slight fall rather than a rise of pressure in the systemic circuit;

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1. Fuhner, H., and Starling, E. H.: Experiments on the Pulmonary Circulation, J. Physiol. **47**:286, 1913-1914.

2. Drinker, C. K.; Churchill, E. D., and Ferry, R. M.: The Volume of Blood in the Heart and Lungs, Am. J. Physiol. **77**:590, 1926.

3. Churchill, E. D.: The Effect of Increased Blood Flow on the Ratio Between Oxygen Consumption and Pulmonary Ventilation, Am. J Physiol. **86**: 274, 1928. Haggart, G. E., and Walker, A. M.: The Physiology of Pulmonary Embolism as Disclosed by Quantitative Occlusion of the Pulmonary Artery, Arch. Surg. **6**:764 (May) 1923. Scarff, J. E.: Pulmonary Blood Pressures: An Experimental Study, Arch. Surg. **12**:591 (Feb.) 1926.

4. Wiggers, C. J.: Observations on the "Effective" Pressure in the Right and Left Auricles, Am. J. Physiol. **33**:13, 1914.

and, secondly, that the blood returning to the lungs is richer rather than poorer in oxygen and presumably has a reduced rather than an increased content of lactic acid. The fall in aortic pressure results from the diminution in peripheral resistance occasioned by opening the fistula. This lowering of the aortic pressure undoubtedly diminishes the fraction of the total cardiac output that returns to the right side of the heart after traversing the coronary circulation.[5] In the experiments to be described the volume of blood actually flowing through the lungs has been determined by the Fick method,[6] and any change in the coronary fraction brought about by the fall in systemic pressure need not be considered in the calculations. That moderate variations in aortic pressure produce no "back pressure" effects through the pulmonary circuit on the pulmonary artery pressure has been shown by Anrep and Bulatao [5] in heart-lung preparations and confirmed by Katz and Wiggers [7] in the intact animal.

The arteriovenous fistula has been used in these experiments solely as a method of increasing the venous return to the heart. The numerous physiologic effects of such a fistula have been admirably studied by several workers,[8] but no experiments are recorded that deal with the effect of such an anastomosis on the pulmonary circulation.

METHOD

Drinker heart preparations [9] were made in cats anesthetized with sodium barbital. Cats so prepared breathe naturally with the heart exposed in an open pericardium sutured to the wall of the chest. A diagram of the complete preparation is shown in figure 1. The tracheal cannula was connected with a closed oxygen metabolism system containing sensitive valves (*H*), a spirometer (*G*) and a soda-lime chamber (*I*). The excursions of the spirometer were recorded on the kymograph (*C*) and gave a direct indication of the consumption of oxygen. Blood samples were taken by right and left ventricular punctures, which may be carried out under direct vision as the heart is fully exposed.

5. Anrep, G. V., and Bulatao, E.: Observations on the Pulmonary Circulation, J. Physiol. **60**:175, 1925.

6. Fick, quoted by Dock, W., and Harrison, T. R.: The Blood-Flow Through the Lungs in Experimental Pneumothorax, Am. Rev. Tuberc. **10**:534, 1925.

7. Katz, L. N., and Wiggers, C. J.: The Influence of High Systemic Blood Pressures on the Right Ventricle and Pulmonary Circuit, Am. J. Physiol. **82**:91, 1927.

8. Holman, Emile: Experimental Studies in Arteriovenous Fistulas: I. Blood Volume Variations, Arch. Surg. **9**:822 (Nov.) 1924. Holman, Emile, and Kolls, A. C.: II. Pulse and Blood Pressure Variations, Arch. Surg. **9**:837 (Nov.) 1924. Holman, Emile: III. Cardiac Dilatation and Blood Vessel Changes, Arch. Surg. **9**:856 (Nov.) 1924. Lewis, T., and Drury, A. N.: Observations Relating to Arterio-Venous Aneurisms: I and II, Heart **10**:301, 1923.

9. Drinker, C. K.: A Useful Heart Method, J. Exper. Med. **33**:675, 1921.

The pressure in the carotid artery (*A*) was recorded by a mercury manometer (*B*). The pressure in the pulmonary artery was obtained by using a special cannula (*E*) inserted directly into the main stem of the artery just beyond the valves.[10] It was connected through a saline system with a manometer (*F*) having an extremely light cork float so that pressure excursions were written directly on the kymograph in centimeters of saline solution.

The arteriovenous fistula was established by the use of a specially blown double glass cannula (*D*), the apertures of which were tied into the femoral artery and vein in the groin. Opening and closing of the fistula were readily accomplished by removing and reapplying delicate artery clips. A saline wash bottle attached to the cannula enabled it to be filled before the start of the experiment and flushed out frequently in order to avoid the clotting that occurred at times despite the fact that heparin had been given intravenously.

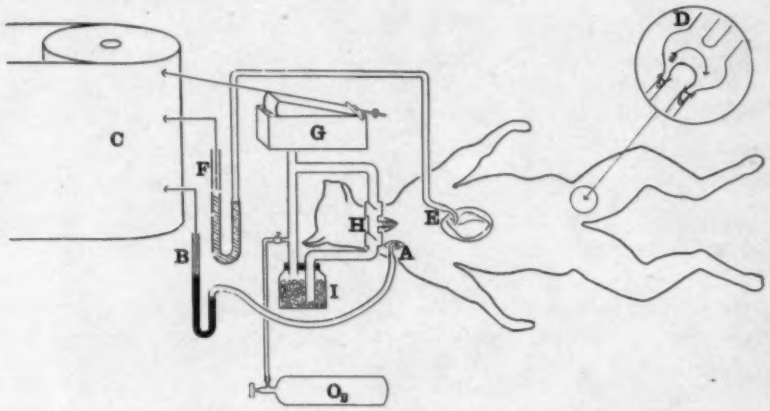

Fig. 1.—Diagram of apparatus, showing: *A*, cannula in the carotid artery; *B*, mercury manometer; *C*, kymograph; *D*, double glass cannula in femoral artery and vein; *E*, cannula in pulmonary artery; *F*, saline manometer; *G*, Krogh spirometer; *H*, inspiratory and expiratory valves; *I*, soda-lime chamber.

PROTOCOL

The following is a protocol of an experiment in which determinations of the blood flow were made.

Experiment 14 (March 21, 1930).—Weight of cat, 3.69 Kg.

10:20 a.m.: Anesthesia induced with chloroform and ether.

10:31 a.m.: 8 cc. of 10 per cent sodium barbital injected into right external jugular vein. Ether discontinued.

10:37 a.m.: Cannula inserted into left carotid artery.

10:39 a.m.: Blood pressure, 144 mm. of mercury.

10:43 a.m.: 2 cc. of sodium barbital injected intravenously.

10. Swift, W. E.; Haggart, G. E., and Drinker, C. K.: A New Method for Measuring the Pressure in the Pulmonary Artery, J. Exper. Med. **36**:329, 1922.

10:47 a.m.: Artificial respiration started for Drinker heart preparation.
11:17 a.m.: Artificial respiration discontinued. Heart preparation complete. Animal breathing naturally.
11:24 a.m.: Double cannula (arteriovenous fistula) tied in left femoral artery and vein.
11:25 a.m.: Tracheal cannula connected with metabolism system.
11:27 a.m.: Rate of oxygen consumption determined.
11:34 a.m.: Blood sample taken from right ventricle.
11:35 a.m.: Blood sample taken from left ventricle.
11:50 a.m.: Cannula inserted into pulmonary artery.
11:55 a.m.: Approximately 100 mg. of heparin in 10 cc. of saline solution injected into femoral vein.
12:09 p.m.: Carotid artery pressure, 116 mm. of mercury. Pressure in pulmonary artery, 18.8 cm. of saline solution.
12:10 p.m.: Arteriovenous fistula opened. Carotid artery pressure, 98 mm. of mercury. Pressure in pulmonary artery, 20.5 cm. of saline solution.
12:11 p.m.: Arteriovenous fistula closed and washed out.
12:19 p.m.: Arteriovenous fistula opened. Consumption of oxygen determined.
12:20 p.m.: Arteriovenous fistula closed and washed out.
12:27 p.m.: Arteriovenous fistula opened.
12:28 p.m.: Blood sample taken from right ventricle.
12:31 p.m.: Blood sample taken from left ventricle.

Experiment ended. Rectal temperature constant at 39 C. throughout the experiment.

RESULTS

The results obtained in experiment 14 were as follows:

Before opening arteriovenous fistula:

Oxygen consumption	= 30.8 cc. per minute
Oxygen capacity of arterial blood	= 16.56 per cent by volume
Oxygen content of arterial blood	= 15.01 per cent by volume
Oxygen content of venous blood	= 6.62 per cent by volume
Difference in oxygen content	= 8.39 per cent by volume
Calculated rate of blood flow (Fick)	= 367 cc. per minute

With open arteriovenous fistula:

Oxygen consumption	= 32.7 cc. per minute
Oxygen capacity of arterial blood	= 13.81 per cent by volume
Oxygen content of arterial blood	= 13.58 per cent by volume
Oxygen content of venous blood	= 7.96 per cent by volume
Difference in oxygen content	= 5.62 per cent by volume
Calculated rate of blood flow (Fick)	= 584 cc. per minute
Increase in blood flow	= 217 cc. per minute, or 59 per cent

The pressure in the pulmonary artery was determined fifty-three times in seventeen experiments both before and after the arteriovenous fistula was opened. There was invariably a slight rise in pressure on opening the fistula and a fall to the previous level on closing. The average rise in pressure was 1.7 cm. of saline solution. The smallest increase was 0.6 cm., and the greatest increase, 3 cm.

Figure 2 is a kymographic tracing showing the effect of opening the arteriovenous fistula on the systemic and pulmonary artery pressures and on the pressure in the left auricle. A cannula inserted into the left auricle was connected with a wide bore saline manometer at the top of which was a small Brodie bellows recorder. The upper tracing

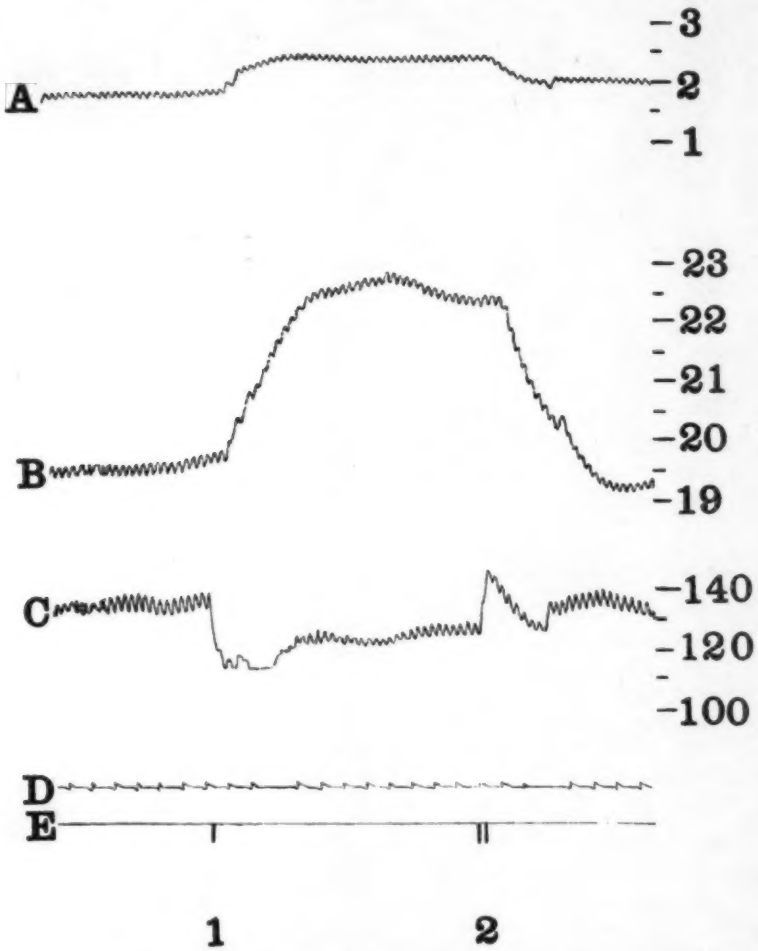

Fig. 2.—Kymographic tracing from experiment 21, showing: *A*, tracing of left auricular pressure calibrated in centimeters of saline solution; *B*, pulmonary artery pressure in centimeters of saline; *C*, carotid artery pressure in millimeters of mercury; *D*, time in 5 second intervals; *E*, signal magnet. At *1* the fistula between the femoral artery and vein was opened. At *2* the fistula was closed.

(*A*) shows the pressure changes in the left auricle calibrated in terms of centimeters of saline solution. The middle tracing (*B*) is that of the pressure in the pulmonary artery, also in centimeters of saline solu-

tion. The lower tracing (*C*) is that of the systemic blood pressure recorded in millimeters of mercury. At *1* the fistula between the femoral artery and vein was opened, and at *2* closed. When the fistula was opened, there was a fall of 10 mm. of mercury in the systemic blood pressure, a rise of 3 cm. of saline solution in the pressure in the pulmonary artery and a rise in left auricular pressure of 0.7 cm. of saline solution.

In five experiments complete determinations of the blood flow were made. The results are tabulated in the accompanying table. It is evident that the circulation rates are below the normal resting levels for cats of similar weight that have not been subjected to operation. This may be attributed to the loss of blood attendant on the operation and the exposure of the heart to atmospheric pressure. The increase in the volume flow of blood through the lungs on opening the arteriovenous

Results of Complete Determinations of the Blood Flow

Cat	Weight, Kg.	Circulation Rate Before Opening Arteriovenous Fistula, Cc. per Minute	Circulation Rate with Open Arteriovenous Fistula, Cc. per Minute	Increase, Cc. per Minute	Per Cent of Increase	Pulmonary Artery Pressure Before Opening Arteriovenous Fistula, Cm. of Saline	Pulmonary Artery Pressure with Open Arteriovenous Fistula, Cm. of Saline	Increase, Cm. of Saline	Per Cent of Increase
5	3.55	268	331	63	24	13.0	14.0	1.0	8
9	2.15	260	376	116	45	19.8	20.8	1.0	5
11	4.13	429	610	181	42	20.5	22.5	2.0	10
14	3.69	367	584	217	59	18.8	20.5	1.7	9
15	3.31	289	409	120	42	14.5	16.3	1.8	12

fistula varies between 24 and 59 per cent in the different cats. The rise in pressure in the pulmonary artery is of slight magnitude in comparison, varying between 5 and 12 per cent. If the resistance in the pulmonary circuit were constant, an increased blood flow through the lungs would cause a proportionate increase in pressure in the pulmonary artery. That the rise in pressure in the pulmonary artery in these experiments was slight and by no means proportional to the increase in volume flow of blood indicates a decreased resistance in the pulmonary circuit. How such a decrease in resistance is brought about has not been demonstrated. It may be attributed to the passive dilatation of the vascular bed of the lungs or to opening of new pathways in response to the increased head of pressure. It is also possible that some mechanism exists that brings about an active change in the tonus and caliber of the pulmonary vessels.

The conditions inherent in the experimental method employed give assurance that the decreased resistance of the pulmonary circuit in these experiments cannot be due to the chemical changes in mixed venous

blood which occur during muscular activity. The arteriovenous communication simulates exercise by increasing the volume flow of blood through the lungs, but paradoxically changes the chemical composition of mixed venous blood in a direction opposite to the changes brought about by muscular activity. The results of these experiments suggest, therefore, that the pulmonary circuit adapts itself to an increased volume flow of blood by a rise in pressure in the pulmonary artery and a lowering of resistance in the pulmonary vascular bed. It seems probable that the latter is a passive phenomenon.

SUMMARY

An arteriovenous fistula in the systemic circuit has been used as an experimental method for increasing the volume flow of blood through the lungs of normally breathing cats. Determinations of the blood flow and measurements of pressure in the pulmonary artery have been made.

In five experiments, the volume flow of blood through the lungs increased from 24 to 59 per cent on opening the arteriovenous fistula.

The pressure in the pulmonary artery invariably showed a slight rise on opening the fistula.

The slight increase in pressure in the pulmonary artery associated with a considerable increase in circulation rate suggests a compensatory lowering of resistance in the pulmonary circuit.

ABSTRACT OF DISCUSSION

DR. JOHN H. GIBBON, JR., Boston: I am glad that Dr. Coryllos spoke of Dr. Wearn's work on the capillaries of the lung. We have not, of course, in this experimental study, determined how the decrease in pulmonary resistance occurs, i. e.: whether it occurs by the opening up of new capillaries or by relaxation of the pulmonary arterioles.

OBSTRUCTIVE PULMONARY ATELECTASIS

PROBLEMS OF PATHOGENESIS AND CLINICAL MANAGEMENT *

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AND
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When bronchial obstruction develops, as by accumulation of mucus from inflamed membranes, and evacuation fails, the air imprisoned in the lung is absorbed and atelectasis results. This has been demonstrated by repeated and well controlled observations in man and in experimental animals. Methods of prevention and treatment aim to free the lower airways from material by stimulating the natural expelling forces or by instrumentation and to aerate the lung with deep breathing. Thus the theory of the pathogenesis and clinical management of obstructive pulmonary atelectasis is clear on the face of it.

When the phenomena are examined in detail, however, they appear complicated and confused. Opposite effects may result from circumstances that are seemingly identical, and this may occur in the same individual simultaneously in separate parts of the lungs. Contradictory results are seen especially in the action of cough on bodies obstructing the bronchi and in collapse of the lung after obstruction. Thus, cough may or may not raise the secretions, and may even drive them farther into the lung; complete bronchial blockage leads quickly to atelectasis on one occasion, and produces no reduction of the pulmonary air content on another.

Our purpose in this paper is to review the experimental and clinical data of obstructive atelectasis so far as necessary to set forth gaps and inconsistencies, and then to indicate a solution to some of these problems by reference to a principle of respiratory function that we have demonstrated recently.[1]

It will be necessary, first, to define and explain certain terms to be used.

Atelectasis refers to an airless state of the lung with collapse of the alveoli. No reference is implied to consolidation by replacement of air with exudate, transudate or other substance.[2] Obstructive atelectasis,

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* From the Department of Surgery, Yale University School of Medicine.

1. Van Allen, C.; Lindskog, G., and Richter, H.: Yale J. Biol. & Med. **2**:297, 1930; work ready for publication.

2. The more inclusive term apneumatosis used by Coryllos (Postoperative Apneumatosis [Atelectasis] and Postoperative Pneumonia, J. A. M. A. **93**:98 [July 13] 1929) carries these implications.

already defined, is distinguished from the compressive type, in which the alveoli are collapsed by pressure from without, and the fetal type, in which there is persistence of the prenatal airless condition. Reference to bronchial obstruction will apply only to that from fluids, for the sake of definite example. The obstruction is referred to as partial when the cross-section of the bronchial lumen is incompletely filled, and air may pass in either direction, as total when the cross-section is completely filled and air cannot pass and as valvular when the arrangement is such as to permit air to pass in one direction only. In the last instance, the valve is spoken of as expiratory when exit is allowed and as inspiratory when entrance is allowed. The position of the obstructing plug in the bronchial tree is indicated as lobar when one or more entire lobes of the lung are shut off thereby, and as lobular when one part of a lobe is occluded. The term distal is used in relation to the bronchial tree to indicate the direction or part toward the alveoli from a given point, while proximal applies to the direction or part toward the trachea. The word air is used loosely to refer to the respired gases in general. The available air is an expression introduced to replace vital capacity, meaning that part of the air in the lung after the deepest inspiration which can be thrown out with one maximal expiration.

THE DEVELOPMENT OF BRONCHIAL OBSTRUCTION

The bronchial tree is provided with various means to maintain its patency, viz., cartilaginous stiffening in the walls of the larger passages, the dilating influence of the pulmonary muscular and elastic tissue, bronchial peristaltic and ciliary action, the ebb and flow of air in quiet or forceful respiration and gravitation.

The bronchi are known to undergo change of caliber synchronously with the phases of respiration, dilating during inspiration and contracting in expiration. The change is increased in forced breathing, and complete obliteration of the lumen may occur with cough [3] or in anaphylaxis.[4] Rhythmical constricting waves have been seen to pass along the bronchi in a proximal direction.[5] To what extent movements of the bronchial wall act to expel material lying in the lumen cannot be told from the evidence obtained, because the result is confused with that of ciliary expulsion. Radiopaque bodies have been seen to pass from the bronchi to the trachea in as short a time as twelve minutes.[6] Theoretically, the bronchial inspiratory enlargement may serve to dis-

3. Weingaertner, M.: Arch. f. Laryng. u. Rhin. **32**:1, 1920.

4. Schultz, W., and Jordan, H.: J. Pharmacol. & Exper. Therap. **2**:375, 1911.

5. Bullowa, G., and Gottlieb, G.: Laryngoscope **32**:284, 1922. Reinberg, S.: Am. J. Roentgenol. **14**:354, 1925.

6. Bullowa and Gottlieb (footnote 5, first reference).

engage the wall from the obstructing body and loosen the attachment, while the expiratory constriction compresses and molds the body to a smaller diameter and squeezes it along the tube.

The eliminative action of the cilia is an entity definitely to be reckoned with, for there is direct evidence of its effects. In patients under general anesthesia, blood stains have been seen by bronchoscopy to travel from the carina to the larynx in a few minutes.[7]

Passage of the respired air in quiet or forced breathing tends to loosen obstructions in its path and to move them along. Emphasis should be placed on the fact that the available air is responsible for

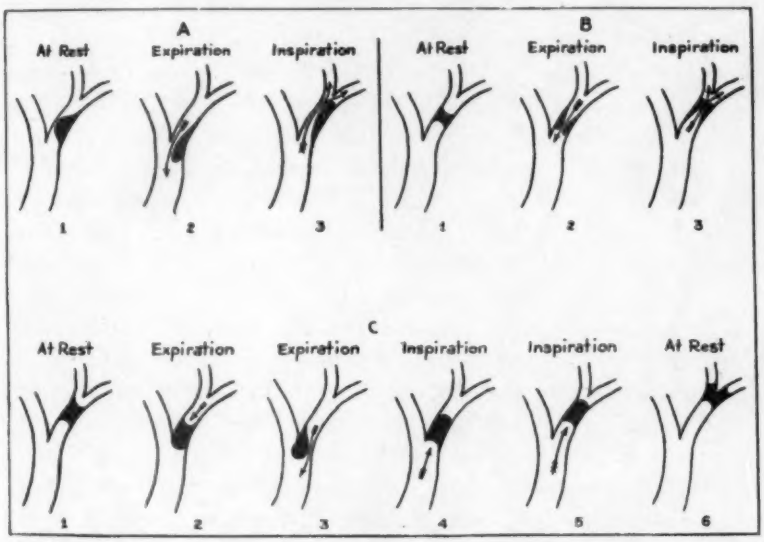

Fig. 1.—Three varieties of the behavior of mucus obstructing the bronchial lumen under the influence of respired air: *A*, partial obstruction; *B*, "doughnut" type of obstruction; *C*, expiratory valve type of obstruction.

the effects, and that the residual air is powerless to operate in an eliminative capacity. Thus an individual is able to execute the muscular effort and laryngeal movements of cough after a complete expiration, but no exclusion is accomplished. The available air is the ram that drives through the bronchi and trachea in coughing; all or a part of this may be used by one cough, depending on excursion and force. Expulsion of substances from the bronchi depends on the expelling force superseding forces of adhesion. The behavior of sticky, viscid fluid in various quantities in the bronchial tree in forced respiration is suggested by reference to figure 1. The drawings at *A* show partial

7. Myerson, M.: Laryngoscope **34**:63, 1924.

occlusion by a small mass lying in the bronchial lumen. With expiration, it is urged in a proximal direction, and it will be thrown toward the trachea if the force is sufficient. With inspiration, it is urged distally and may be transported into smaller passages, where total obstruction may result. At *B*, a larger mass fills the bronchial lumen at one point when at rest, but the amount is small enough and adhesion strong enough that at expiration and inspiration thinning and rupture occur at the center, and the result is a partial occlusion.[8] At *C*, a still larger accumulation is present. Expiration pushes it along the bronchus to a point of sudden and considerable enlargement of the lumen at the entrance of a side branch. Sufficient force being active, it will be carried past this to become a partial obstruction in the larger passages beyond; but if adhesion is the greater force, the mass may ride at the bifurcation while the air passes and drop back again at inspiration, refill the lumen and be carried into the periphery. This event, however, has brought about partial or complete loss of the available air from that part of the lung, and the plug now assumes a position higher than before, or, if it resists distal displacement, suction is developed on its distal side in each inspiratory phase. Expiration is less able than before to effect expulsion in proportion to the amount of available air lost. The event may have had yet another result, for the cross-sectional area of the bronchial tree increases rapidly toward the periphery, and a plug that fills the lumen of a given bronchus may be unable to fill more than a part of its branches. The phenomenon of transportation of obstructions toward the periphery has been observed in man and in animals by the aid of fluoroscopy and the injection of iodized poppy seed oil 40 per cent.[9] It may be explained in part by the expiratory valve mechanism that has been described and in part by absorption of air distal to the obstruction and changes in pressure relationships from that source. Thus figure 2 gives curves of pressures that were obtained from the bronchial lumen at points just proximal and distal to a total plug occluding one lobe. Only the expiratory pressures are shown, and the purpose of the experiment was to determine the influences exerted by quiet and forceful breathing on a total plug. There was quiet respiration to begin with, and section *A* represents the two pressures when obstruction was instituted during expiration and loss of a part (tidal) of the available air. The levels are seen to be practically identical. At *B*, obstruction was relieved temporarily and then instituted at the height of inspiration. The inspired air was thus imprisoned behind the plug. The distal pressure

8. This is the "doughnut" behavior described by Lee (personal communication) from bronchoscopic observations in man.

9. Archibald, E., and Brown, A.: Am. Rev. Tuberc. **16**:111, 1927.

level is seen to be above that of the proximal pressure. The situation was allowed to remain for observation, and it was found that the distal pressure gradually fell and in thirty minutes had reached the level of the proximal pressure. Presumably, the tidal air was being absorbed or otherwise lost. After this, the effect of cough was imitated by shutting off the trachea momentarily in the early stages of expiration and obtaining straining. Both pressures are seen to rise sharply, the proximal pressure to somewhat the higher point. The domination of

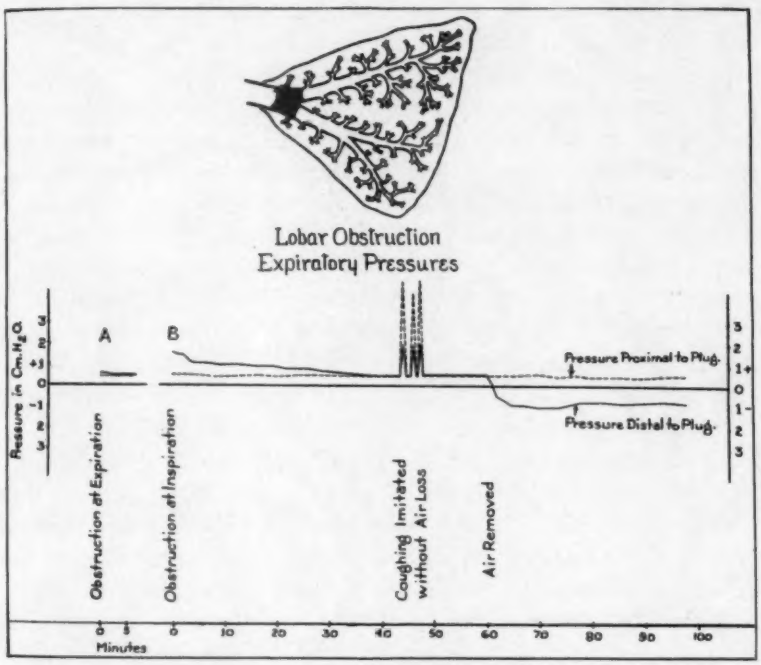

Fig. 2.—Plug producing complete lobar bronchial obstruction. Curves of expiratory pressures measured at points proximal and distal to the plug. Obstruction instituted at the end of expiration (*A*) and at the end of inspiration (*B*).

the proximal value was found to be a constant effect of straining to expire against resistance and to be proportional to the exertion of straining. After this maneuver the pressures returned to their former levels at equality with each other; when they were noted to remain without noticeable change for a few minutes, about 5 cc. of air was withdrawn by aspiration with a syringe from the occluded portion of the bronchial tree. The distal pressure is seen to drop at once below the proximal pressure and to maintain the lower level. These measurements show that in expiration the relation of the pressures distal and proximal to a bronchial obstruction filling the lumen totally at one

point depends on the amount of air imprisoned distal to the plug, and that the distal pressure predominates only when air previously inspired still remains. It has been found [10] that the distal pressure drops progressively as the imprisoned air is absorbed and atelectasis develops. The degree of suction then exerted on the plug toward the periphery of the lung is considerable. Under conditions of lowered distal pressure, coughing serves to increase the predominance of the proximal pressure.[11] Coughing can therefore be expected to expel a total plug only when a supply of air available for its action exists in the occluded portion of the lung, and this supply tends to be absorbed. With loss of the available air, cough is calculated to exert a driving effect toward the periphery.

This evidence of the dependency of cough and other expiratory functions on the available air of the obstructed portion of the lung for expelling effects appears to be directly contradicted by certain clinical experiences. Reliable observers [12] have reported that some patients with well developed massive atelectasis have been relieved of the condition after violent coughing and deep breathing. Thick, tenacious mucus was coughed up at the time, and roentgen examination showed re-aeration of the lung. This contradiction will be discussed further after other problems have been presented.

THE DEVELOPMENT OF ATELECTASIS

Credit belongs to Lee and his associates [13] for the first satisfactory proof of the obstruction theory of atelectasis.[14] They occluded a part of the bronchial tree of a dog with thick mucus which had been aspirated from the bronchus of a patient with atelectasis, and they found that the corresponding portion of the parenchyma of the lung was atelectatic after three hours. Concentrated mucilage of gum acacia was used for the same purpose in four other dogs, and atelectasis was evidenced within from thirty minutes to three hours.[15] Coryllos, Hen-

10. Van Allen, C., and Adams, W.: Surg. Gynec. Obst. **50**:385, 1930.

11. Lindskog, G., and Van Allen, C.: Work ready for publication.

12. Scott, W. J. M.: Massive Atelectasis and Postoperative Pneumonia: Prophylaxis and Treatment, J. A. M. A. **93**:101 (July 13) 1929.

13. Lee, W.; Ravdin, I.; Tucker, G., and Pendergrass, E.: Ann. Surg. **88**:15, 1928.

14. Lichtheim (Arch. f. exper. Path. u. Pharmakol. **10**:54, 1878) is commonly credited with the first experimental reproduction of obstructive atelectasis. He confused atelectasis with pneumonia, however, and permitted pneumothorax collapse of the lungs to enter into the circumstances of experiment to such an extent as to render the results unconvincing.

15. Complete proof, by postmortem examination, of the presence of atelectasis in their animals was obtained (personal communication to the authors), although a report was not published.

derson and their co-workers [16] obstructed the primary bronchus on one side in about sixty dogs with inflated rubber balloons and examined the lungs after a period of time which varied from one to twenty-four hours. Atelectasis of the occluded part was always found. Still others have obtained this condition after closure of the bronchus to one or more of the pulmonary lobes by ligature.[17]

Convincing evidence in denial of this causal relation of bronchial obstruction to atelectasis came to one of us (C. V. A.[10]) in earlier work. The first was seen in a dog that was being used in experiments for another purpose. Two months before, the wall of a bronchus within the lower lobe of the right lung had been cauterized through a bronchoscope and completely destroyed for a length of about 1 cm. The lobe now presented the picture seen in figure 3. The bronchus was interrupted at the burned point by a solid sequestrum of necrotic tissue, and beyond this the bronchial lumen was filled throughout with glassy mucus, as evidence of total obstruction. Nevertheless, the parenchyma was air-containing (fig. 4) and could not be distinguished in this regard from that of unoccluded portions of the lung. In two other instances of the same sort, in which examination was made one and one and one-half months, respectively, after destruction of a bronchus, the lung again remained normally air-containing.

Other methods for obstructing the bronchi were then tested. Gum acacia mucilage, of the concentration used by Lee and his co-workers, was injected into the bronchial tree or the lower lobe of the right lung, and the dogs were maintained under anesthesia in order to depress the respirations and to ensure retention of the material. Three animals were so treated and then examined after a period of from three to twelve hours. No atelectasis resulted, although the bronchi remained "drowned" with the fluid. The rubber balloon method was rejected because of difficulty with deflation, and instead a certain sticky and malleable rubber preparation (Michelin mastic) served the purpose well. Piece after piece of this was carried through a bronchoscope and pressed into the bronchi of the lower lobe of the right lung and accessory lobes, until they were distended with a branching cast which presented no possibilty of slipping and admitting air. This type of obstruction was applied to four dogs and permitted to remain for

16. Coryllos, P. N.: Postoperative Apneumatosis (Atelectasis) and Postoperative Pneumonia, J. A. M. A. **93**:98 (July 13) 1929. Coryllos, P. N., and Birnbaum, G. L.: Obstructive Massive Atelectasis of the Lung, Arch. Surg. **16**:501 (Feb.) 1928; Lobar Pneumonia Considered as Pneumococcic Lobar Atelectasis of the Lung, ibid. **18**:190 (Jan.) 1929. Henderson, Y.; Haggard, H. W.; Coryllos, P. N.; Birnbaum, G. L., and Radloff, E.: Treatment of Pneumonia by Inhalation of Carbon Dioxide, Arch. Int. Med. **45**:72 (Jan.) 1930.

17. Andrus, W. DeW.: Cardiorespiratory Physiology Following Collapse of One Lung by Bronchial Ligation, Arch. Surg. **10**:506 (Jan.) 1925.

periods up to twenty-four hours before the animals were killed. No atelectasis resulted.

The total variety of bronchial plug had thus failed after trial in different forms in ten dogs, and a test of obstruction was next made by means of an apparatus that had the effect of an expiratory valve. A dog was anesthetized and tracheotomized, and a cork, pierced by a tube, was slipped down the trachea and forced into a bronchus of the

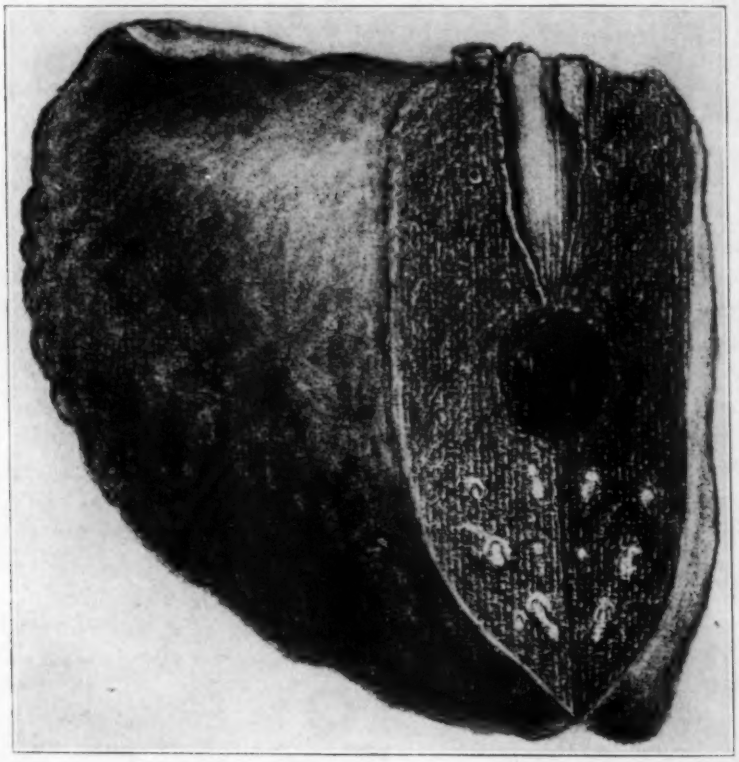

Fig. 3.—Right lower lobe of a dog's lung. The bronchus has been opened, demonstrating complete lobular obstruction of the lumen caused by cauterization two months before the animal was killed. The bronchial tree distal to this point is filled with retained mucous secretion, and the parenchyma is air-containing.

lower lobe of the right lung. From this cannula a slender rubber tube was carried out of the trachea and connected to a glass nozzle. The tip of the nozzle was submerged just below the surface of water in a vessel. With first expiration air bubbled past the water valve in considerable quantity; with the second, a bubble or two passed, and after this (the available air having escaped) the bubbling ceased. The water meniscus in the nozzle fell with each expiration precisely to the level of the outlet, and rose about 10 cm. with inspiration. These levels

remained constant, as nearly as could be detected, for six hours. At autopsy, the cork was found so tightly engaged in the bronchus that the tissues had to be cut to free it, and yet the obstructed portion of the lobe was fully air-containing. Three other dogs treated in this way behaved similarly.

In an experiment of this type with a cork and water valve the tracheotomy opening became partly closed by a blood clot. This was not discovered until it had been in effect for some time and had given rise to labored respiration. After four hours, the animal was killed; autopsy revealed complete atelectasis of the obstructed lobe of the

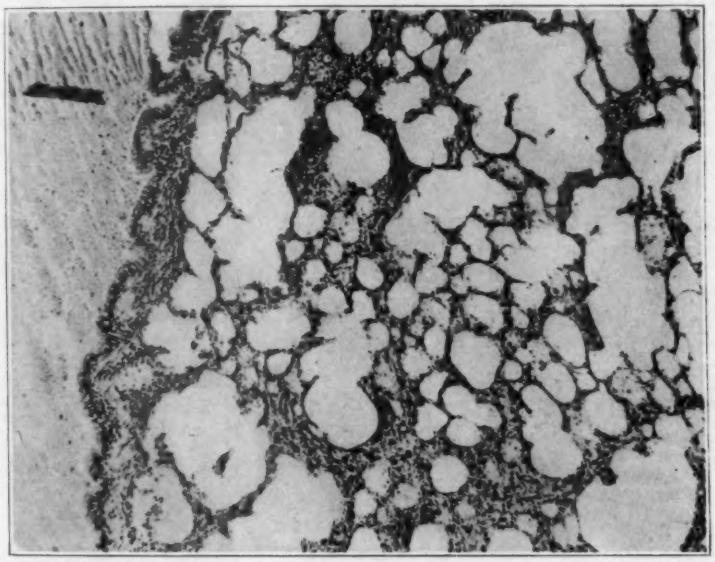

Fig. 4.—Microscopic appearance of the parenchyma of the lung specimen shown in figure 3, in the obstructed part. The alveoli are air-containing, and at one side is a bronchus filled with secretion.

lung. The factor of resistance in the trachea was then applied to other dogs, impediments of other sorts being substituted for the blood clot, such as gauze sponges or partial closure of the trachea by clamping. Atelectasis formation then became the rule. Analysis of the situation showed that the effect was obtained by resistance applied to the expired air passing through the trachea, and the type of respiration thus produced appeared similar essentially to that of coughing, moaning, grunting, etc., in which the vocal cords approximate and resist expiration. We have referred to this as straining respiration. Its presence in these experiments was found essential to the development of atelectasis, whether the plug was total or equipped with a valve, and the

reason for this remained undetermined. The valve, indeed, played no part other than to permit the available air to escape and to hasten by so much the advent of atelectasis.

After this, the apparatus [18] and method for occluding the bronchus were refined, to permit more precise selection of the point of occlusion and reduction of trauma. It became possible to apply obstruction to various parts of the bronchial tree and more precisely than hitherto; immediately confusion entered into the results, for straining respiration then failed in some instances to effect atelectasis. In some experiments atelectasis developed, and in others in which no difference existed that could be detected, except for the position of the plug, the lung remained perfectly air-containing. Analysis of a series of tests showed that atelectasis occurred when the plug involved one or more lobes (lobar obstruction) and failed when only a part of one lobe was included (lobular obstruction). This is illustrated by the roentgenogram reproduced in figure 5. Three of the pulmonary lobes are depicted after removal from a dog twenty-four hours following the application of two bronchial plugs (surgical bone wax introduced by bronchoscopy). The plug at *A* is lobar and that at *B* is lobular. Atelectasis appears only at *A*. A review of previous experiments now disclosed the fact that when record had been made of this point the instances of atelectasis were those with lobar obstruction. The cause for the difference in the results of lobar and of lobular obstruction was not at once apparent.

The situation presented by our data up to this time, regarding the factors of the type of respiration and the position of obstruction, is summarized in figures 6 and 7. The amount of atelectasis produced and the period of time of each bronchial plug used are represented by a single dot or circle. Figure 6 refers to experiments with free respiration throughout, and the dots indicate lobular, and the circles lobar, plugs. It is seen that atelectasis occurred in lobar obstruction only, and not until, after twenty-four hours. Under these circumstances, however, the occurrence was not constant. Figure 7 presents the experiments with straining respiration, and the same designation of lobular and lobar positions is used. Atelectasis is noted again in lobar obstruction only, but here it is seen to have appeared to some extent in nearly all cases and to have reached extensive developments, often at early periods.

The results of these experiments demonstrate, further, that aside from the influence that the type of respiration and the position of the obstruction exert, the incidence and rate of atelectasis formation after total bronchial occlusion in a twenty-four period are variable to the extent of 100 per cent. No explanation for this has been found.

18. Van Allen, C.: Yale J. Biol. & Med. **2**:295, 1930.

THE PRINCIPLE OF AIR EXCHANGE BETWEEN THE PARTS OF A LOBE

Certain deductions from these experiments have led to other experiments and the demonstration of a principle of respiratory function which pertains to the behavior of air in the lung beyond a bronchial obstruction and which serves to explain some of the contradictions at hand. Details of the proof and character of this are furnished elsewhere.[1] The principle may be stated briefly as follows:

Fig. 5.—Roentgen appearance of three lobes of a dog's lungs after bronchial obstruction by wax plugs for twenty-four hours. *A*, complete lobar obstruction, followed by atelectasis; *B*, complete lobular obstruction, with maintenance of aeration. A test with high pressure showed these plugs to be air-tight.

The partitions that divide one alveolus from another and one lobule from the next in a single lobe of a lung permit air, fluids and finely particulate matter to pass. This exchange is a result of very slight differences in pressure within two adjoining lobules (the difference may be as low as 1 cm. of water pressure); these differences are such as are commonly generated between obstructed and free parts of the bronchial tree during quiet breathing. It has been found that an

obstructed portion of one lobe "breathes" by means of this communication through adjacent free parts, and that the amount of this respiratory interchange may be as much as 3,600 cc. per hour. The interchange is found to occur in man, the dog, cat and rabbit by tests made in vitro. The methods for testing during life are applicable to the dog only, and in this animal the phenomenon is regularly obtained. It fails to occur between lobes.

The mechanism of this passage is not clear. Diffusion may account for it, but the fact that a particulate substance (india ink) is admitted indicates that there must be anatomic connections. These are evidently

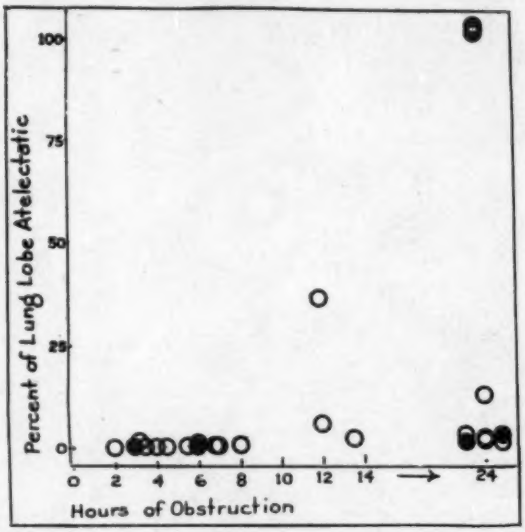

Fig. 6.—Results of twenty-five experiments with bronchial obstruction in the presence of quiet breathing. The amount of atelectasis produced and the period of obstruction in each case are indicated by a single dot or circle. Dots refer to complete lobular obstruction and circles to complete lobar obstruction.

in the periphery of the lung, and they may be the alveolar wall pores recently described by Ogawa [19] as to position, shape and construction.

INTERPRETATION

The free intercommunication that exists between the anatomic units of a lobe of a lung appears to play a determining part in the mechanism of both bronchial obstruction and atelectasis formation. To assist in understanding the function, an analogy may be drawn to the exchange of fluid by anastomosis in the blood and lymph vascular systems, which

19. Ogawa, C.: Am. J. Anat. **27**:333, 1920.

permits one unit to compensate for interruption that may occur in the supply channel of the other. In the bronchial system of one lobe, blockage of a part leaves others to ventilate the parenchyma. This compensation fails when all bronchi of a lobe are occluded (lobar obstruction).

The inconsistencies appearing in the action of cough are removed by consideration of this circumstance. As has been emphasized, cough depends for eliminative effect on the presence of available air in the lung behind the bronchial obstruction. The inspiration that precedes the cough furnishes air to the obstructed lung past the plug, if that is

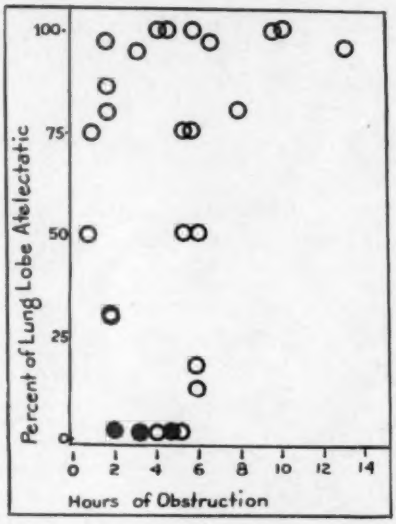

Fig. 7.—Results of twenty-seven experiments with bronchial obstruction in the presence of straining respiration. The same method of designation is used as in figure 6.

partial or of the inspiratory valvular type, or by way of the peripheral intercommunications, if the plug is total and lobular. Under these circumstances, the cough builds up a higher pressure in the bronchial lumen distal to the plug than in that proximal to it, and may move the obstruction toward the larynx. This is illustrated by the curves shown in figure 8, from pressures measured at points just distal and proximal to a total lobular bronchial plug. The expiratory pressures only are shown. The distal pressure lies above the proximal value, and this relationship persists during quiet respiration throughout. When the action of cough was imitated, both pressures rose abruptly and fell, producing an increase in the advantage of the distal value. Again, on the removal of about 10 cc. of air from the bronchial tree beyond the

plug, no disturbance resulted in the relation between the two pressures. This behavior contrasts with that of the air in a lobar total plug, as has been described (fig. 2), for then the inspiration that precedes the cough does not furnish air to the obstructed lung, and if the available air already in that part has been lost by absorption or other means, the cough is unable to raise the distal pressure above the value proximal. It should be remarked that this distinction between the lobular and the lobar positions of obstruction in the effectivity of cough refers as well to lobular plugs that are with and without functioning intercommuni-

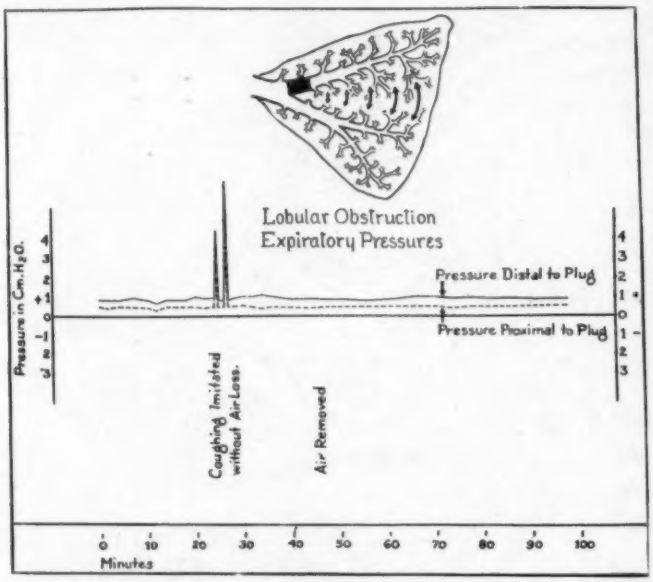

Fig. 8.—Plug producing complete lobular bronchial obstruction. Curves of expiratory pressures measured at points proximal and distal to the plug. Obstruction was instituted at the end of inspiration.

cation. Thus it has been found that one part of a lobe may become isolated by a multiplicity of mucous plugs, so that the behavior of the imprisoned air is the same as that in lobar obstruction.

The importance of the peripheral intercommunication for routine maintenance of the patency of the bronchi is evident when one contemplates the extreme fineness of the peripheral airways, the lack of mural rigidity and of ciliary apparatus and the tendency to secretion and exudation. A minute drop of fluid must serve to obstruct a respiratory duct. Were it true, as generally believed, that the duct ends in a blind cluster of alveoli, consider the situation that arises

when the duct becomes occluded during sleep or at other times when expelling forces are not soon instituted. The available air would soon be absorbed, and the opportunity for expulsion of the block would be lost. The obstruction must remain. As it is, with exchange of air between the alveoli, expulsion is possible with each expiratory effort. As a matter of fact, during shallow respiration the communications may not function after bronchial blockage, and the part remains isolated until a deep breath or two is taken. After that, exchange of air is instituted and continues in effect. This has been a common observation, and may be explained by supposing that the alveoli in some parts are not used in shallow breathing and partly collapse, with the result that they cannot serve for the purpose of intercommunication without first a full inspiration to expand them. The deep breath or yawn that follows on prolonged quiet occupation or on awaking from sleep may have the purpose of expanding functionless regions of the parenchyma for the aeration and unburdening of occluded parts.

The development of atelectasis following bronchial obstruction must depend primarily on the rate of two processes, i.e., loss of air and accession of air. When the rate of loss is in excess, atelectasis results. The questions of the position of the obstruction and the efficiency of the peripheral communications are therefore of prime importance. Atelectasis may develop only when the obstruction is lobar or when it is lobular and the communications to that portion of the lung are partly or wholly closed and unable to keep pace with loss of air by absorption or other means. A total lobular plug in normal communication with free adjacent lobules has not been seen to result in atelectasis, and this consideration appears to explain the failure of atelectasis formation in lobe *B*, figure 5, as well as many of the other failures in our work to obtain this condition after bronchial obstruction.

No explanation, however, has yet been obtained for the marked accelerating influence of straining respiration on atelectasis formation. In addition, there remain unexplained the marked differences in the rate of atelectasis formation that are to be seen when both the position of the obstruction and the type of respiration are kept constant. There must be important factors still unrecognized which enter into the pathogenesis of the condition, in one instance to speed absorption of air and in another greatly to delay or to stop it. Since absorption of air is by the blood stream,[10] these factors probably relate to that, and improvement in the circulation or its retardation would be expected to hasten or to slow absorption of air. Investigations along this line are under way.

CLINICAL APPLICATION

We have no additions to make to the measures of prevention and treatment already in practice. However, these deserve discussion as to advisability, with reference to the principles of bronchial obstruction and atelectasis formation already explained. Another circumstance of great importance requires attention: the infection that precedes and accompanies atelectasis in most instances. Bacterial or chemical inflammation of the bronchi is usually responsible for obstructing secretions and exudates; and to infection are due in large part the distressing symptoms and dangerous complications of atelectasis. That the dyspnea, fever and prostration are immediately related to the infection, rather than to collapse of the lungs, is strongly suggested by the facts that compressive atelectasis, as in pneumothorax, produces relatively slight cardiorespiratory disturbance and no toxemia, and that obstructive atelectasis in the dog does not give rise regularly to any of these effects. The loss of function of so much lung is probably unimportant in itself in most cases. Attention has been directed in the recent literature to the complications of atelectasis and particularly to pneumonia. While there is no direct and convincing evidence [20] that atelectasis represents the first stage of pneumonia, or even that it predisposes to pneumonia, there is little doubt that the serious bronchitis that leads to massive atelectasis may readily progress to pneumonia.

In applying to clinical use the knowledge of atelectasis that has been gained, caution is advisable lest by active intervention, calculated to be beneficial in one respect, actual harm is done by transgression of principles not yet understood. Care should be taken, also, not to aggravate the accompanying infection. Indeed, conservatism may well be indulged in for the present, as atelectasis in massive proportions is unusual, its morbidity brief and fatality from the condition itself rare.

For preventing the accumulation of inflammatory products in the bronchial tree, recourse may be had to medication and to encouragement of natural forces for elimination from the bronchi. Inhibition by drugs of the mucous secretions is indicated in nonbacterial irritations of the tract, as in inhalation anesthesia, and it has little place, if any, in well developed infectious bronchitis. Inhalation of steam is beneficial in moistening and warming the inflamed surfaces. Of the eliminative forces, the ciliary and peristaltic functions may be aided by attention to their two main impediments, i.e., the suction that follows absorption of air distal to a total obstruction, and adverse gravitation. Fluids

20. The hypothesis advanced by Coryllos and his associates, designating atelectasis as a constant precursor and disposer to pneumonia, as yet lacks any direct anatomicopathologic proof. They have demonstrated no more than the frequent juxtaposition of the two conditions.

accumulating in the bronchial tree tend to settle first of all in the smaller passages, and the earliest total obstruction is likely to be lobular. At this stage it should be possible to prevent collapse of the lung in the obstructed parts by maintaining aeration of the free portions of the lobe and permitting intercommunication at the periphery. This may be done by means of an occasional deep breath. Even after isolation of the part has become complete, as in lobar obstruction, deep breathing may still be effective, since the plug in one or another of the passages may be of small size and admit air by inspiratory dilatation of the bronchus, by thinning and rupture at the center or by being sucked into the periphery and leaving some of the small branches free. Here again, it should be appreciated that an occasional deep breath or two is sufficient. Continuous hyperpnea, as induced by inhalations of carbon dioxide,[21] is probably unnecessary and may be tiring. The added muscular exertion called forth, reflex and subtle though it may be, must require output of energy. As a matter of fact, when massive obstruction has been reached, dyspnea and cyanosis (high carbon dioxide content of the blood) are often already at hand and require no augmentation. The impediment to the eliminative functions by gravitation is, of course, readily replaced by equally effective assistance from that source, by placing the patient's head at a level below the bases of the lungs. Coughing should be used in moderation, since its action is not always effective and may be harmful. The chief benefit from the cough is to be expected in the removal of partial obstructions, and the action becomes uncertain in total obstructions. The ciliary and peristaltic forces are mainly to be relied on in the latter condition. On the other hand, it is clear that coughing has a somewhat irritating effect and, in addition, tends to accelerate the absorption of air that is imprisoned in the lung. Excessive spontaneous coughing should be controlled. It must be remembered that rest is important to the general resistance of the patient in combating the coincident infection.

The following plan of procedure is suggested for routine use in preventing the development of bronchial occlusion.

Elevation of the foot of the bed is the only constant addition to the ordinary nursing and general supportive measures. If it is evident that bronchial secretions are excessive, a regular schedule is adopted, with a change of side in the lying position and with encouragement to inspire deeply and to cough once or twice. Hourly or half-hourly intervals are used. When suggestion is not effective or desirable to obtain the inspiration and cough, as in sleeping, unconscious or otherwise uncooperative patients, inhalations of carbon dioxide should be

21. Henderson, Haggard, Coryllos, Birnbaum and Radloff (footnote 16, fourth reference).

substituted. Breathing of steam is used if specially indicated. Sedatives are administered freely and in amounts to control spontaneous coughing that occurs in excess, and to obtain rest.

Once physicial signs and symptoms indicate that atelectasis has occurred, suction is operating to draw the offending plug toward the periphery, and all forces of expulsion are at a disadvantage, particularly that of cough. Also, any straining in breathing acts to accelerate absorption of the pent-up air that still remains, and respiratory exercises that contain this element are to be minimized.[22] The effects of air hunger and toxemia are also added to the picture. Bronchoscopic aspiration of the obstructing material has been demonstrated to have a place in the treatment for this condition, for in numerous reported cases [23] the atelectatic lung has returned to a normal roentgenologic appearance and the symptoms have disappeared after the removal of mucus from the bronchi. There is usually an immediate aeration of a part of the lesion, and the remainder then becomes air-containing, section by section. Relapse may occur at any stage. It is often impossible to unburden all the branches of a lobe by aspiration, nor is that necessary. The steplike aeration described is probably due to a progressive process of inflation through the periphery from one respiratory unit to the next. Thus, after bronchoscopic treatment and liberation of one or two branches, the patient immediately inspires into and aerates the corresponding part of the lobe. From this, in turn, the air may be inspired by way of peripheral communications into adjacent portions that are still obstructed. This serves to inflate the parenchyma lying distal to the remaining bronchial plugs, to relieve the suction and to provide available air for the action of cough; clearance of the rest of the obstruction proceeds spontaneously by cough. It should be emphasized, however, that bronchoscopy in other than highly skilful hands may add materially to the acute tracheobronchitis and bring about more damage than benefit. The rate of bronchial secretion may be accelerated and relapse encouraged thereby; cases are on record that required repeated bronchoscopic intervention. It then becomes a question whether the patient is afforded greater peace and security from the intermittent engagements with the endoscopist than he would be if allowed to pursue the natural course of the condition under conservative management.

The routine treatment for atelectasis may be planned to follow the same measures that have been suggested for prevention.

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22. Attention is called to the fact that deep breathing has not been found to fall into the category of straining respiration, unless there is resistance to expiration, as in coughing, grunting, moaning, etc.

23. Lee, W.: Work ready for publication.

SUMMARY

The present understanding of the pathogenesis and clinical management of obstructive pulmonary atelectasis is reviewed to set forth certain problems:

1. The inconstant action of cough and other natural eliminative forces in maintaining and effecting clearance of the lower respiratory passages.

2. The uncertainty of incidence of atelectasis formation after bronchial obstruction.

3. Irregularity of the rate of atelectasis formation.

Solution is offered for some of these problems by reference to certain principles of respiratory function recently determined:

1. Exchange of air between parts of a lobe at the periphery.

2. The accelerating influence of straining respiration on the rate of absorption of air in the occluded part of the lung.

3. The dependence of cough for its eliminative effect on the presence of available air in the occluded part of the lung.

It is pointed out that the third problem, which concerns the rate of atelectasis formation, remains partly unsolved.

Evaluation is made of the methods in vogue for the prevention and treatment of atelectasis.

ALVEOLAR GAS EXCHANGES AND ATELECTASIS

THE MECHANISM OF GAS ABSORPTION IN BRONCHIAL OBSTRUCTION *

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Physiology
- Requirements of Gas Exchanges
- Solubility, Diffusion and Osmosis
  - Solubility Coefficient
  - Diffusion Pressure
  - Osmotic Pressure
- The Dissociation Curve of Hemoglobin in Relation to Respiration
- The Regulation of Respiration and Circulation
- Composition of the Alveolar Air
- Venous Blood

Experimental

Technic
- Intrabronchial Cannulas
- Closed Chest Experiment
- Open Chest Experiment

Material and Purpose of Investigation

Problems Investigated
- Fate of Alveolar Air Entrapped in a Pulmonary Lobe After Complete Occlusion of Corresponding Bronchus
- Changes Produced in Entrapped Alveolar Air as Indicated by Successive Gas Analysis
- Is Entrapped Air Absorbed and at What Rate?
- Speed of Absorption of Gases of Alveolar Air Introduced Individually in Atelectatic Lung of Living Animal and Gas Exchange That Takes Place Thereafter
- Results Following Introduction of Neutral Gases Separately Into Atelectatic Lung
- Behavior of Respiratory Membrane Toward Anesthetic Gases or Vapors
- Changes, if Any, in Intrapulmonary Pressure in Occluded Lung During Process of Absorption
- Absorption of Various Gases by the Lung
  - Closed Chest Experiment
  - Open Chest Experiment

Our Theory of Production of Atelectasis

Comment

Conclusion

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* From the Department of Surgical Research, Cornell University Medical College. This work was aided by a grant from the National Research Council and a gift of Mrs. John L. Given in support of surgical research.

In previous papers we have endeavored to present clinical and experimental evidence in favor of the theory that atelectasis is always produced by complete bronchial obstruction, including those cases in which it follows collapse of the lung from compression as in open or tension pneumothorax or abundant pleural effusion.

If we have repeatedly and persistently dealt with this subject, it is because we consider that it is of greatest practical importance that atelectasis should be associated in the mind of the practitioner with bronchial obstruction, and that he should seek out its cause by further investigation of the bronchial tree. We believe that he must accept as an axiom that whatever may be the conditions favoring the production of atelectasis—impairment of pulmonary ventilation, narcotics, postoperative splinting of the thoracic cavity because of pain, posture, decrease of cough because of narcotics or pain, previous common colds, etc.—there is but one immediate cause, complete bronchial obstruction. Roentgenographic and often bronchoscopic examinations are necessary to establish the particular cause of the disease in a given case. To cite only a few examples, many latent foreign bodies, tumors of the mediastinum and, more particularly, many tumors of the lung (which in a great majority of cases are of bronchogenous origin) might be discovered in this way. It is obviously desirable to diagnose such tumors in their earliest stages when they are still operable. Then again, in the cases of nonopaque foreign bodies in children, in prolonged forms of postoperative atelectasis and even in hemoptysis with sudden symptoms of impending asphyxia, a knowledge of the obstructive nature of atelectasis would be of the greatest importance for the initiation of appropriate treatment. Last but not least, with the idea of the relation between bronchial obstruction and atelectasis always in mind, the thoracic surgeon in carrying out collapse therapy or resection of a lung for chronic suppuration of the organ will adopt preventive measures or will have always at hand the necessary instrumentarium for treating bronchial obstruction due to pus expressed from the collapsed lung. Many fatalities after chest operations believed due to postoperative shock are simply due to obstructive atelectasis, as is clearly shown by a careful perusal of case histories cited in the literature (Berry and Lambert). It is only reasonable to suppose that a good number of these deaths might have been prevented even after such an accident had happened. Had the necessary measures been known and readily available, advantage could have been taken of that short period which intervenes between the moribund state of the patient and death for reestablishment of respiration. So long, however, as we content ourselves with such hazy explanations as "vasomotor reflex," "bronchomotor reflex" or "angioneurotic edema," no real effort will be made to avoid or treat the real and tangible cause of atelectasis, which we repeat, is bronchial obstruction.

Obstructive atelectasis or apneumatosis of the lung is generally admitted to be produced by absorption by the circulating blood of the air entrapped in the alveoli. Lichtheim gave an experimental demonstration of this fact in 1879 by plugging the bronchi of rabbits with laminaria or spongewood and noticing the absorption of air. Furthermore, he showed that oxygen is absorbed much more quickly than air. This theory is, of course, not upheld by those authors who believe in the mechanical expulsion of alveolar air by capillary engorgement (vasomotor reflex theory) or edema of the alveoli (angioneurotic edema).

More recently, Rappaport (November, 1929) completely rejected the theory of the absorption of alveolar gas by the blood. He endeavored to explain the production of obstructive atelectasis by a mechanism of "respiratory decompensation" leading to a "plethora of the lung." "Failure in function of one lung," he said, "results in the production of excessive plethora which finally floods the air passages and produces atelectasis. . . . The mechanism of production of atelectasis . . . is either failing respiratory function by way of direct immobilization or by way of excessive compensation, which fails." He added, "As to the bronchial plug theory, I think it is untenable, that it is not even worth discussion. . . . Bronchial obstruction causes only bronchial emphysema . . . the conception of absorption of the air behind the plug is all wrong." For the foregoing statements, this author offers no experimental proof. "I have no such evidence," he said, "mine is purely clinical."

On the other hand, Van Allen and Adams, in a recent (February, 1930) purely experimental paper, arrived at the following conclusions:

1. Even complete bronchial obstruction does not lead to atelectasis in the normal lung if the animal breathes quietly; straining respiration is essential to the production of atelectasis.

2. Pent up bronchial air is "probably" lost from the lung by absorption by the blood stream. "It is a curious circumstance," said these authors, "that air which is imprisoned within the normal lung under conditions of quiet respiration remains without absorption for a long time, if, indeed, it is ever absorbed, whereas air introduced into the neighboring pleural cavity or into the tissue spaces elsewhere tends quickly to disappear. Perhaps the query is more pertinent as to why air, and especially the nitrogenous part of it, at any point should be absorbed." In the experiments, however, in which these authors plugged the bronchus leading to the lower right and to the accessory lobes but in which the branch of the pulmonary artery leading to the accessory lobe only was ligated, the lower lobe (with intact pulmonary artery) was deflated and atelectatic, whereas the accessory lobe (the pulmonary artery of which was ligated) "was air-containing and of normal appear-

ance." This seems, to us, characteristic evidence of the production of atelectasis by absorption of the alveolar air by the circulatory blood, because only in this way the necessity of circulatory integrity in its production would be understood. Van Allen and Adams do not discard the theory of alveolar gas absorption, but, on the other hand, they do not definitely admit it because of the apparent difficulty with this theory to explain their failure to produce atelectasis in quiet respiration. They therefore compromise: "Those experiments," they said, "designed to test the part played by the blood stream in atelectasis formation, must be guarded as to interpretation. In ligating the vessels the nerves to the lung may also have been injured, and the failure of air absorption under these circumstances may have been due to either or both of these effects."

We have quoted from these two papers because they represent, so to speak, the extreme wings of the series of papers on atelectasis published during the last two years both in America and abroad, which cast doubt on the mechanism of production of this disease by bronchial obstruction and absorption of the alveolar gases by the blood. The first is a purely clinical paper without any attempt at experimental verification of the statements and theories advanced. The second is purely experimental. Both, however, have one point in common: They express doubt as to absorption of alveolar air by the blood circulating in the alveolar capillaries. It would seem that the solution to the whole question lies in the answer to this question: Is the alveolar air absorbed by the blood, and if it is, what is the mechanism of this process? It is obvious that the answer to the question and the solution of the problem will be necessary to establish the obstruction theory on a solid and indisputable physiologic basis; but once this proof has been given, we feel that the other theories usually advanced would be dealt a definite blow and should be discarded.

The rationale for determining the exchange of gases in the lung in relation to atelectasis is thus apparent. The task was difficult, complicated and full of pitfalls. It required a great deal of specific knowledge and complicated experimentation, of extreme precision in the quantitative determination and many precautions and continuous check-ups in the interpretation of the results obtained. The experiments were long, often lasting twelve, fifteen, twenty or even forty-six hours, during which time many details required coordination and constant supervision; among these details were the occluding balloon, the pleural cannulas, the roentgen apparatus, the oscillating vacuum source, the manometers and recording devices, etc. During these long hours the animals were put to the hard test of deep narcosis and intrabronchial manipulation. We had to face many disappointments in order to "carry

on" for over a year. On the other hand, the problem was so captivating and the results obtained of such great interest that no effort seemed too great.

We feel that the data to be presented definitely uphold the production of atelectasis by complete bronchial obstruction and absorption of the alveolar air, and that they can explain the pathogenesis of this disease without the additional help of "straining respiration," "valvular expulsion," "respiratory decompensation," or "respiratory failure" (with or without "lung plethora"), "angioneurotic edema," "vasomotor reflex," etc.

PHYSIOLOGY

Since our problem is based entirely on physiologic grounds and in close relation to the physics and chemistry of respiration and the exchange of respiratory gases, it is necessary, for a full comprehension of the underlying details, to make some ingress into the fascinating but also often desperately complicated question of respiration. Modern conceptions on respiration have modified the older theories in many ways. On the other hand, in the painstaking work of many of the older physiologists, especially of Pflüger, Ludwig and their pupils, we found much relevant material precious to our own work. The prominent controversy concerning the function of the alveolar respiratory membrane lasted for over fifty years; the last word on the subject has not yet been said. Is it a simple semipermeable membrane through which the exchange of gases proceeds according to the laws of diffusion as maintained by Pflüger, at the head of Bonn's laboratory, or is it a true secretory epithelium secreting oxygen much as salivary epithelium secretes saliva, as Ludwig and his pupils at the Leipzig Laboratory maintained? Many papers of great significance and accuracy were published during that heroic period of study on the respiration. Although almost completely forgotten today, they are in general accord with the fundamentals of the modern physiology of respiration. Among these older works and under titles apparently bearing no relation to our problem, we were indeed surprised to discover that bronchial obstruction was carried out previously on the dog (Wolffberg, 1871) and even on man (Loewy and von Schroetter, 1905). The object of these authors was to determine the exact composition of the gases of the alveolar capillary blood by analyzing the entrapped alveolar air, since in from five to fifteen minutes after bronchial obstruction an equilibrium sufficient for their purpose in gas percentages is established between the alveolar gases and the gases in the venous capillaries of the lung. Our results are in complete accord with those given by these authors, as we shall later see.

Requirements for the Exchange of Gases.—Respiration is the exchange of gases between alveolar air and venous alveolar blood on the one hand, and between the tissues, lymph and capillaries on the other hand. The exchange of gases in the lung—the only one which interests us at present—requires the following conditions: (1) the integrity of the endothelial membrane composed of the alveolar and capillary endothelium which separates the alveolar air from the venous capillaries of the lung; (2) the difference in partial pressures of the gases present on either side of this membrane; (3) the integrity of pulmonary ventilation with the continuous renewal of the alveolar air which is only possible if there is no interference with the patency of the air passages from the larynx to the respiratory bronchioli, atria and ducti alveolaris, and (4) the integrity of the intrapulmonary circulation.

No one of these conditions can be altered without producing profound changes in the mechanism of the exchange of gases.

It is easy to understand how edema or inflammatory thickening of the alveolar membrane will impair or stop this exchange. Likewise an unhampered circulation is essential for the normal exchange of gases. The blood being the normal and only gas carrier in the organism from the lungs to tissues and vice versa, it is obvious that impairment or interruption of the pulmonary circulation will preclude or bar completely the usual exchange of gases. Likewise, an efficient ventilation is just as essential. It is the sine qua non condition for maintaining the gases on either side of the alveolar membrane under those conditions of different partial pressures which are absolutely essential for the exchange of gases. In fact, the most important factor in the accomplishment and regulation of the exchange of gases is the difference in partial pressures of the gases in the alveolar air and in the venous alveolar capillaries. As Paul Bert first showed, it is not the total pressure of the gas mixture, but the partial pressure of each individual gas, each acting as if it were alone, which is of importance in physiology. In a mixture of gases, when no chemical action occurs, each gas behaves independently. Dalton has shown this fact and formulated the law of partial pressures which bears his name. Thus if 100 cc. of oxygen and 400 cc. of nitrogen both at one atmosphere of pressure are mixed, the resulting mass of gas occupies 500 cc. at the same pressure; but the oxygen acts as if it were under a pressure of only one fifth of an atmosphere ($\frac{1}{5} \times 760 = 152$ mm. of mercury), while the nitrogen acts as if it were under a pressure of four fifths of an atmosphere ($\frac{4}{5} \times 760 = 608$ mm. of mercury).

Solubility, Diffusion and Osmosis.[1]—We shall be obliged to use physiochemical terms such as solubility coefficient, diffusion and osmotic pressures, etc. A short explanation of these terms will therefore be useful.

Solubility Coefficient.—Solubility of a gas in a liquid depends on the nature of the gas, the nature of the solvent, its pressure and the temperature. The solubility of hydrogen, oxygen, carbon dioxide in 1 cc. of water at 15 C. and at 760 mm. of mercury pressure are: hydrogen, 0.019; oxygen, 0.0342, and carbon dioxide, 1.002. The solubility of the different gases is not the same in different solvents, but the order of solubility of gases in different liquids is almost always the same.

The solubility of a gas in a given solvent, such as water, is appreciably diminished by the presence of dissolved solids or liquids, especially electrolytes. According to Philip, the presence of solids diminishes the solubility of gases because a part of water enters into combination with the solute and is thus made unavailable for absorbing the gas. Solubility of a gas increases with increased pressure and decreases with elevation of temperature. Furthermore, concerning the nature of the gases, those which present basic or acid reactions are much more soluble than the neutral ones as, for example, the case of carbon dioxide compared to nitrogen. But the predominant factor in the solubility of a gas is, again, pressure. According to Henry's law: "The weight of a gas dissolved in a liquid is proportional to the pressure of the gas." One should not, however, confuse "weight" and "volume." Since volume and pressure at a constant temperature are inversely proportional (Boyle's law), the law of Henry may be stated thus: "The volume of a gas absorbed by a given volume of liquid is independent of the pressure," but the weight of the gas absorbed is, of course, proportionately increased. Dalton has shown that the solubility of individual gases in a mixture of gases, is directly proportional to their partial pressures, the solubility of each gas being independent of the pressure of the others.

From these considerations, it follows that the concentration of the dissolved gas is directly proportional to the concentration of the gas in the free space above the liquid. In fact, when a definite volume of liquid is saturated with a gas at a constant temperature and pressure, a condition of equilibrium is established between the gas in solution and that over the solution. If C_1 represents a concentration of gas in the liquid, and C_2 the concentration in the free space, we have the equation: $\frac{C_1}{C_2} = K$, where K represents the solubility coefficient.

1. An excellent summary of the physiochemical aspects of the question will be found in Getman's "Outlines of Theoretical Chemistry," ed. 4, New York, John Wiley & Sons, 1928.

Diffusion Pressure.—If a cylinder containing hydrogen is placed mouth to mouth on a cylinder containing oxygen, although hydrogen is sixteen times lighter than oxygen, after a short while we shall find a perfect mixture of the two gases. Hydrogen has diffused against the laws of gravity into the oxygen.

If a few cubic centimeters of a concentrated solution of cane sugar is placed in the bottom of a tall cylinder and water is added, care being taken to prevent mixture, the sugar immediately begins to diffuse into the water, until the concentration of sugar is the same throughout the liquid. The sugar molecules move from a region of high concentration to a region of low concentration and diffuse into the water.

In the case of gases the rate of diffusion is extremely rapid. For the hydrogen molecule this speed is 1,840 meters per second or faster than a rifle bullet. The average speed for oxygen under the same condition is one fourth of this value or 460 meters per second. Thus the "rate of diffusion of gases is inversely proportional to the square root of the density of the gas."

In solution the process of diffusion is much slower. But the molecules obey the same fundamental laws, and they are explained in the light of the same theory—the molecular kinetic theory. If the solution and the pure solvent are separated by a semipermeable membrane which is permeable to the solvent and not to the solute molecule, the latter will exert a pressure on the membrane as a result of their successive impacts on it. In dilute solutions "the diffusion pressure" follows the gas laws.

Osmotic Pressure.—Osmosis is the diffusion of a liquid through a membrane. When a salt solution, for example, is separated from water by a suitable animal membrane, the water diffuses through the membrane more rapidly than the salt. The level of the salt solution rises causing an appreciable hydrostatic pressure to develop. Since this pressure is caused by the process of osmosis it is called the "osmotic pressure."

The osmotic pressure of a solution is not to be regarded as an actual pressure exerted by a component of the solution (solvent or solute) but rather as the difference in pressure which must be established between the solution and solvent, respectively, in order to render the escaping tendency of the solvent equal to that of the solution. According to the molecular kinetic theory, if pure water is placed on both sides of a semipermeable membrane which allows the passage of the solvent only but not of the solute, the molecules of water being in ceaseless motion will bombard the membrane from both sides. But when the molecular concentration (number of molecules in a unit of space) on both sides is the same, it is obvious that as many molecules will pass through the

membrane in one direction as in the other and that no osmotic pressure will develop.

If now, instead of pure water a solution is placed on one side of the semipermeable membrane, it is obvious that the number of molecules of water present in it in a unit of volume is less than in the pure solvent. Under these new conditions, the number of molecules of solvent passing through the membrane in a unit of time will be less for the solution than for the pure solvent. Thus the equilibrium is disturbed in favor of the pure solvent and this difference in pressures constitutes the osmotic pressure. On the other hand, the molecules of the solute tend to diffuse into the pure solvent. But as the molecules of the solute cannot pass through the semipermeable membrane, a pressure develops which represents the diffusion pressure of this particular substance.

It is interesting to point out here that equimolecular quantities of different substances dissolved in equal volumes of the same solvent exert the same osmotic pressure and produce the same relative lowering of

TABLE 1.—*Osmotic Pressure of Cane Sugar Solutions*

C	P	$\frac{P}{C}$
1	53.5	53.5
2	101.6	50.8
4	208.2	52.0
6	307.5	51.2

vapor pressure. Since equimolecular quantities of different substances contain the same number of molecules, it is evident that the magnitudes of osmotic pressures and relative lowering of vapor pressures are dependent on the number of dissolved units present in the solution and are independent of the nature. In the same way, Pfeffer showed that the osmotic pressures increase with the concentration, to which they are proportional. In table 1, C denotes the concentration of the solution, P, the corresponding osmotic pressure expressed in cubic centimeters of mercury, and $\frac{P}{C}$ the ratio of osmotic pressure to concentration.

It is clear from the figures in table 1 that the osmotic pressure is proportional to the concentration of the solution since $\frac{P}{C}$ is approximately constant. The osmotic pressure exerted by any substance in solution is the same as it would exert if it were present as a gas in the same volume as that occupied by the solution.

We have gone rather extensively into the question of osmotic pressure because it is desirable to show that diffusion or osmotic pressures are not small forces as might easily be believed. They represent tremendous energies, for we have seen that the diffusion rate of hydrogen exceeds the speed of a rifle bullet and, as shown in table 1, the osmotic pressure

of a 6 per cent cane sugar solution is equal to 307.5 cm. of mercury, that is, over 4 atmospheres. It is really marvelous how these forces act in our organism in such a smooth and coordinated way.

The surface of the human lungs, according to Zuntz, is 90 square meters or about 1,000 square feet. During quiet breathing, 300 cc. of oxygen and about the same quantity of carbon dioxide diffuse through in one minute. If the whole surface were used for diffusion, the amount of gas passing per minute through 1 square centimeter would be only 0.0003 cm. and could be accomplished, according to Exner, with a partial pressure of only 1 mm. of mercury.

It is necessary, however, to remark here that the velocity of diffusion is not only inversely proportional to the square root of its density, as we have previously said, but also that it is proportional to the coefficient of solubility of the gas in the fluid concerned. That is why the speed of diffusion of carbon dioxide through a wet membrane is thirty times greater than for oxygen, although its density is greater. This can be easily shown by tying closed a frog's lung filled with oxygen or atmospheric air and placing it in an atmosphere of carbon dioxide. Within a minute the lung is distended, owing to the diffusion of carbon dioxide into it, for the coefficient of solubility of carbon dioxide is thirty times greater than that of oxygen.

Oxygen and carbon dioxide are not merely dissolved in the plasma of the blood. The bulk of oxygen and carbon dioxide is in chemical combination in the blood. The first combines with hemoglobin, the second with alkali.

The Dissociation Curve of Hemoglobin in Relation to Respiration.—The oxygen-hemoglobin compound has the property of dissociating with a fall in the partial pressure of oxygen; this dissociation is complete when the oxygen pressure is reduced to zero. In this way hemoglobin represents an oxygen reserve in the red cells which maintains constant the amount of oxygen dissolved in the plasma, the latter representing the vapor-pressure above an oxygen solution.

Besides the partial pressure of oxygen in the alveolar air or tissues, another important factor in the dissociation of oxy-hemoglobin is carbon dioxide. Increase in carbon dioxide hastens the dissociation of oxygen; it "shifts the dissociation curve of oxy-hemoglobin to the right" and thus facilitates the unloading of oxygen into the tissues as the carbon dioxide in the blood increases. Although this is strictly correct, it is, according to Haldane, of much less importance than the shifting of the carbon dioxide absorption curve in consequence of the reduction of hemoglobin.

In fact, decrease of oxygen in the blood and hemoglobin unsaturation increase the capacity of the blood for carbon dioxide probably

because reduced hemoglobin is a more alkaline substance than oxygen-saturated hemoglobin. The latter acting as a weak acid keeps carbon dioxide out of combination with alkali. Whatever the cause of this action may be, it is certain that saturation of hemoglobin decreases the capacity of blood for carbon dioxide, the result being that with high oxygenation the partial pressure of carbon dioxide in the blood rises although its percentage remains the same. For this reason more carbon dioxide is given off by the blood when its oxygen saturation is high (Werigo, Bohr and Halberstadt). Now it follows that if one lung is ventilated with a neutral gas as nitrogen, and the other with air, the latter will give off nearly 50 per cent more carbon dioxide than the former.

Decrease in carbon dioxide has another important result, discovered by Bohr (1904) and called the "Bohr effect." Such a decrease shifts the dissociation curve of hemoglobin to the left so that whereas in the venous blood (carbon dioxide, 45 mm. of mercury; oxygen, 40 mm. of mercury) the hemoglobin is 68 per cent saturated, if carbon dioxide falls to 10 mm. of mercury, the hemoglobin (without any increase in the oxygen pressure) becomes 85 per cent saturated. Furthermore, the oxygen is more firmly held in combination with hemoglobin so that notwithstanding this apparent increase in oxygen pressure and absence of cyanosis, the oxygen available to the tissues is greatly diminished.

The Regulation of Respiration and Circulation.—In a previous paper on "Circulation in the Consolidated Lung," we stressed the point of perfect parallelism between ventilation of the lung and its circulation. We showed by injecting the pulmonary artery in the living animal with iodized poppy seed oil 40 per cent and the capillaries with india ink in Ringer's solution, that atelectasis as well as other varieties of pulmonary consolidation are accompanied by shrinkage of the alveoli and by shrinkage and collapse of the alveolar capillaries. Not only do these two processes advance hand in hand, but they are also reversible; collapse of the alveolar capillaries following ligature of the pulmonary artery produces shrinkage of the alveoli which ultimately leads to atelectasis and inflation of the lung increases blood flow through the lung. The question that interests us now is how this regulation occurs and by what mechanism this synchronism is insured.

"At bottom," said Haldane, "the regulation of the circulation is a chemical regulation, just as in the case of breathing." Circulation and respiration are regulated by the metabolic requirements of the tissues, which requirements in the last analysis are represented by the partial tensions of oxygen and carbon dioxide or more exactly, by the hydrogen ion concentration in the tissues. Circulation seems to be so regulated as to keep the pressures of oxygen and carbon dioxide approximately

steady in the venous blood of any particular origin. During muscular work, for instance, where a rise of carbon dioxide and fall of oxygen pressure is produced, an increase in blood flow through the muscles follows, with a corresponding increase in venous blood pressure (Henderson and Haggard, 1918). Krogh has shown that under resting conditions the great majority of capillaries in muscular tissue are contracted and impermeable to blood, so that neither blood corpuscles nor the finest particles of india ink can pass through them. Nor is the full arterial blood pressure capable of forcing them open. Whenever the tissue is stimulated to activity, however, these capillaries open wide so that blood can pass through them freely. "It seems that increased oxygen and carbon dioxide production with increased hydrogen ion concentration is the natural stimulus bringing about an increase in local circulation; the regulation of the respective oxygen and carbon dioxide pressures, disturbed by the increased activity of the muscles, is thus brought about." Once the fundamental fact is grasped, said Haldane, that the general flow of blood throughout the body is correlated with gas pressures in the capillaries, the whole physiology of the circulation appears in a new light. "In fact, so long as the contractions of the ventricles are complete, the volume of blood discharged at each beat must depend on the extent to which the right ventricle fills in diastole. This in turn depends on the rate at which blood is let through from the arteries to the veins. It is therefore the rate at which the systemic blood is allowed to pass through the tissues into the venous system that determines the amount of blood pumped by the heart; and as already pointed out, the rate at which blood is allowed to pass through the tissues is determined by their metabolic requirements. It is evident that in this regulation by both the heart and the blood vessels the nervous system plays an important part, just as in the case of regulation of breathing; but the main fact must never be lost sight of, namely, that the primary factor determining the rate of circulation is neither the heart nor the nervous centers, but the metabolic activities of the tissues. This is exactly what Claude Bernard meant when he said in his "Leçons sur les phénomènes de la vie" that "all the vital mechanisms, varied as they are, have only one object, that of preserving constant the conditions of life in the internal environment" (the blood).

Henderson and Haggard, in a series of papers on "Acapnia and Shock," showed that a condition can be brought about in animals by excessive ventilation of the lungs which washes out the carbon dioxide and produces a state of alkalosis with slowing of the circulation and consequent great anoxemia. The slowing of the circulation tends, as Haldane remarked, to "diminish the alkalosis in the tissues but only at the expense of producing most formidable anoxemia."

Anoxemia and alkalosis persist, and shock is produced as the circulation rate decreases, and the heart fails.

However, the condition of shock might be produced by an altogether different mechanism, especially in postanesthetic conditions In these cases, as Van Slyke, Van Slyke, Austin and Gullen, Ronzoni, Leake and others have shown, instead of an alkalosis as in acapnia, there is always a more or less pronounced degree of acidosis with decrease in alkali reserve, a decreased partial pressure of carbon dioxide in the alveolar air and an increased hydrogen ion concentration (low p_H). This condition, which is similar to the condition frequently observed in cases of nephritis and diabetes due to nonvolatile acids, has been described by Hasselbach and Gammeltoft as "uncompensated acidosis" and by Van Slyke as "uncompensated alkali deficit." The carbon dioxide (in the form of carbonic acid) is high and not decreased in proportion to the fall of blood bicarbonate. As Leake and Henderson pointed out, it seems extremely plausible that this acidosis might be due to defective sugar oxidation. "Among the essential factors of an efficient oxidation of sugar are: Adequate supply of sugar, an ample supply of oxygen and sufficient insulin to facilitate the process. Deficiency in any of these factors leads to withdrawal of alkali from the blood into the tissues. In the dynamic equilibrium of this process the mass action of oxygen is balanced against the mass action of bicarbonate ion and the hydrogen ion concentration is a variable dependent (through respiration) upon the ratio of oxygen to sodium bicarbonate and tending to restore that ratio to normal by the shift of alkali from blood to tissues and vice versa" (Henderson). There is thus a close parallelism between the percentage of oxygen and the amount of alkali in the blood which might explain how anoxemia can produce "uncompensated alkali deficit." It would therefore seem possible that between anoxemia and postoperative acidosis there exists a relation of cause and effect. It is not within the scope of this paper to enter into this topic, which will be dealt with in a forthcoming paper. We only wish to point out here the relation existing between deficient sugar oxidation, acidosis, hypoventilation and postoperative pulmonary complications (atelectasis). It would seem not to be a mere coincidence that these complications are most frequently present after operation on the upper part of the abdomen; probably exposure of the liver, exhaustion of sugar reserves, disturbed insulin production and decreased ventilation have a part in their production. This condition of hypoventilation favors "respiratory stagnation" and leads to atelectasis by facilitating bronchial retention and obstruction and thus to the absorption of alveolar air by the venous blood circulating in the perialveolar capillaries.

In order to present all the elements necessary to the complete comprehension of this problem, it is essential to deal with the composition of alveolar air and the gases of the venous blood.

Composition of the Alveolar Air.—The composition of the alveolar air, analyzed according to the method of Haldane and Priestley, can be considered, in normal persons at rest and at average barometric pressure, as follows: oxygen, 15 per cent; carbon dioxide, 5 per cent; nitrogen, 80 per cent. (Haldane's figures are: carbon dioxide, 5.6 per cent; oxygen, 14.5 per cent.) In order to simplify the question, we are going to consider 760 mm. of mercury as the normal pressure in the lung. In reality, the alveolar air being saturated with water vapor, the actual gas pressure is 760 —47 = 713 mm. of mercury, 47 mm. of mercury being the tension of water vapor; the effect of the negative intrapleural pressure (of from 5 to 8 mm. of mercury) is negligible. Knowing the percentage of the different gases, we can easily calculate their respective partial tensions: oxygen is $^{15}/_{100} \times 760$ mm. = 114 mm. of mercury; carbon dioxide is $^{5}/_{100} \times 760$ mm. = 38 mm. of mercury; and nitrogen is $^{80}/_{100} \times 760$ mm. = 608 mm. of mercury.

It is understood that the foregoing figures are only approximate and represent composition of the air contained in the air sacs. From here toward the outside (atria, bronchioli, bronchi, trachea and larynx) the respiratory air approximates more and more the composition of atmosphere air, that is, oxygen, 20.95 per cent; carbon dioxide, 0.03 per cent; nitrogen, 79.02 per cent; so that in analyzing the expired air one finds it poorer in oxygen and richer in carbon dioxide as specimens are taken deeper in the lung. As one follows the gases from alveolar air and arterial blood to venous blood and to the lymph of the tissues, the oxygen gradually decreases and the carbon dioxide increases.

The alveolar air is separated from the venous blood by the endothelium of the air sacs and of the capillary vessels which cover their external surface and by a negligible amount of extremely thin elastic and smooth fibers. In some species, as in birds, there intervenes only a vascular endothelium, because there is not a real respiratory epithelium but only a homogeneous hyaline membrane—an extremely thin film. Through this respiratory membrane the exchange of gases between alveolar air and the venous capillaries takes place.

Venous Blood.—There is a great variation in the figures given by different authors in the composition of the gases contained in the venous blood in contrast to the figures for arterial blood, which are remarkably constant. We shall use the figures given by Loewy and von Schroetter for man, to which the figures given by Henderson and Haldane approximately correspond: oxygen, 5 per cent; carbon dioxide, 6 per cent. These correspond to the following partial pressures:

oxygen, 38 mm. of mercury, and carbon dioxide, 45.6 mm. of mercury. The partial pressure of nitrogen is the same as in the alveolar air, 608 mm. of mercury, although its percentage is extremely low.

The question of gas pressures in the venous blood and more particularly in the venous capillaries of the lungs is of paramount importance. The exact determination of these pressures is not an easy task. Two methods are generally used: One is a direct analysis of the venous blood taken from the right ventricle; the other is an indirect determination by one of the following methods: the "hose method" of Haldane and Priestley or the "bronchial plugging" method of Siegfried Wolffberg. The latter, less well known and seldom reported, bears an important relation to our work. The rationale of this method is that if a bronchus is occluded, the air entrapped in it will after a while reach an equilibrium with the gases of the venous capillaries, so that a quantitative analysis of this air is equivalent to a gas analysis of the venous blood. Becher (1855) and F. W. Müller (1870) tried to realize this

TABLE 2.—*Results of Gas Analysis (Wolffberg)*

Duration of Obstruction of the Bronchus, Minutes	Amount of Gases in the Alveolar Air, 100 Vol. of Gas	
	Carbon Dioxide	Oxygen
1.0	1.7	4.3
2.0	1.9	3.1
5.0	3.8	3.0
6.5	4.2	2.7

equilibrium by the voluntary holding of respiration. But, as Donders remarked, a short suspension of respiration is not sufficient to establish an equilibrium between alveolar air and blood gases, whereas, on the other hand, a prolonged cessation will cause an increase of carbon dioxide in the blood. We shall give a detailed description of the method of Wolffberg which is similar to ours, although used for a different objective. Loewy and von Schroetter applied a similar method to man (1905).

Wolffberg, working in Pflüger's laboratory (1871), used the lung catheter of Pflüger (fig. 1). With this catheter he was able to obstruct a bronchus for a time varying from three to ten minutes. He introduced this catheter in the trachea of dogs, previously tracheotomized, without anesthesia. The terminal balloon of the catheter was then inflated, thus plugging the chosen bronchus; but through the central tube of the catheter the investigator was connected with the alveolar air and was able to draw a specimen of air for analysis. His method and results are extremely significant. We give his results in table 2.

The figures in table 2 show clearly that carbon dioxide increases and oxygen diminishes proportionately to the duration of occlusion until an

approximate equilibrium is obtained, at which time the composition of the venous capillary blood can be deduced from the percentages of gases present in the obstructed lung.

The same question was studied in a similar way by Loewy and von Schroetter in a truly monumental work on respiration. These authors experimented directly on human beings by producing a temporary obstruction of a bronchus. The determination of the exact tension of gases in the alveolar air after a bronchial obstruction sufficiently prolonged to establish an approximate equilibrium of gas between alveoli and blood, enabled them to calculate the amount of oxygen carried by the arterial blood and the amount of oxygen utilized in the organism, the

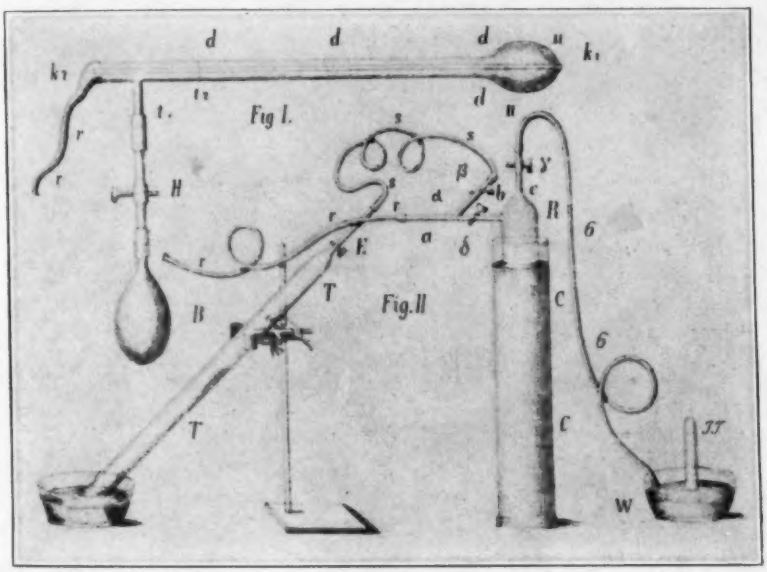

Fig. 1.—Pflüger's lung catheter (fig. I) and gas analysis apparatus (fig. II), used by Wolffberg for bronchial obstruction and analysis of the entrapped alveolar air. The catheter is composed of an elastic tube, *dddd*, which terminates in an elastic balloon, *uu*. This catheter is known in obstetrics as the Tarnier catheter used for inducing premature labor. At the end of the catheter a glass T tube (t_2) was introduced, the vertical branch of which (t_1) was connected with a rubber bulb (*B*) which could be separated from the catheter by a stop-cock (*H*). A fine glass tube, k_1k_2 is introduced through the horizontal branch of the glass tube into the catheter and the balloon (*u*) at the tip of which a hole is made through which the tube can pass to the outside. The posterior half of the horizontal branch of the T tube is filled with cement around the fine glass tube, so that the latter leads from the entrapped alveolar air to the outside; once the catheter is introduced in a bronchus and the balloon (*u*) inflated, samples of air can be taken for analysis.

blood velocity, the heart output and finally the work of the heart. Their technic consisted in introducing into the trachea of the patients a special obstructive apparatus similar to the lung catheter of Wolffberg (fig. 2). Its introduction was accomplished through the tracheal fistula in tracheotomized patients, or in other patients, through the mouth by means of the bronchoscope, using local anesthesia with cocaine applied to the laryngotracheal mucosa as in the usual bronchoscopy. Their catheter was composed of two silver tubes 1.5 and 0.7 mm. in diameter, fixed together to allow an easy passage through the glottis or through a tracheal fistula. At the distal end an elastic balloon was attached in

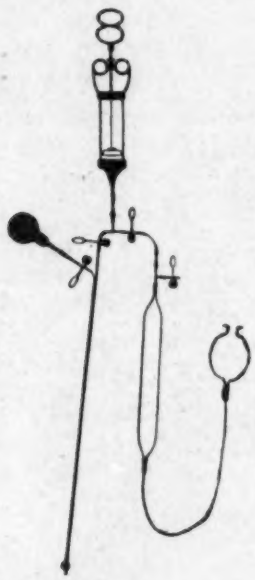

Fig. 2.—Lung catheter of Loewy and von Schroetter. On the left side is the catheter, with the terminal balloon; it is a double metal tube, one tube being connected to the balloon and the insufflating bulb, and the other with the entrapped alveolar air on the one hand, and with the apparatus for taking gas specimens, figured in the right side of the picture, on the other. Between them is adapted a syringe for aspirating the entrapped air and sending it into the gas-sampling apparatus (from Loewy and von Schroetter).

such a manner that it could be insufflated through the smaller of the tubes, whereas the other (larger) tube was terminated below the balloon and it was in communication with the pulmonary air below the obstruction. The other end of this tube was connected with a rubber tube, closed by a stop cock, from which samples of air could be drawn by a syringe from the occluded lung for analysis. The oral end of the small tube was connected with an insufflating bulb for inflation of the

bronchial balloon. Both tubes could be passed in an air-tight manner through a T form mouth valve (somewhat similar to that used in basal metabolism) which was connected with a spirometer and an inspiratory valve for measuring the expired air coming from the nonplugged lung (figs. 3 and 4).

For the introduction the authors used the following technic: The right bronchus was always used because of its more vertical direction. After cocainization of the larynx, the bronchoscope was introduced. A site in the right bronchus was selected for the obstruction. The distance of this site from the upper teeth was carefully measured on the bron-

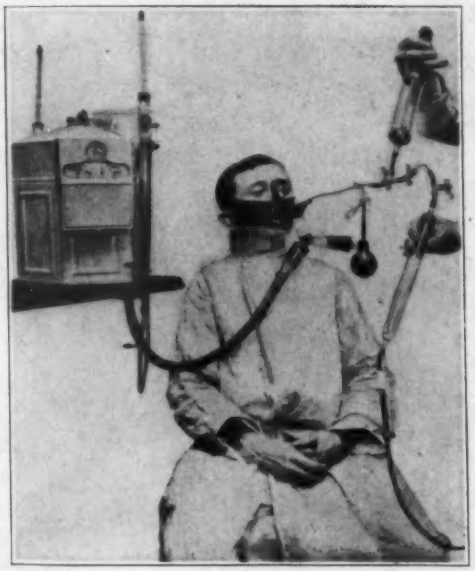

Fig. 3.—The Loewy and von Schroetter lung catheter introduced through the mouth and trachea into the right stem bronchus. To the apparatus is connected a mouth valve which is connected to a spirometer (from Loewy and von Schroetter).

choscope, and the instrument was removed. Then by the use of a tongue spatula, the patient being seated with the head in hyperextension, the epiglottis was retracted, the glottis seen and the lung catheter gently introduced into the right bronchus so that the balloon was at exactly the distance previously recorded through the bronchoscope. The balloon was then inflated and the mouthpiece, if necessary, put in place. After a few trials the patient was accustomed to the apparatus, so that Loewy and von Schroetter were able to maintain the apparatus in place for as long as forty-two minutes. Specimens of gas were drawn every

minute or so from the oral end of the tube, so that it was possible to follow the successive modifications brought about in the composition of the entrapped alveolar air.

The time necessary for the establishment of an equilibrium between the gases of the blood and alveolar air, according to Wolffberg, was short, only a few minutes for dogs. In the experiment on man by Loewy and von Schroetter, this was generally obtained within from six to seven minutes. Loewy and von Schroetter found that the size of the occluded part of the lung has little importance for the rapidity of establishment of the equilibrium. It even seems that when an entire

Fig. 4.—The same lung catheter (Loewy and von Schroetter) as in figure 3. The apparatus is introduced into the right stem bronchus through the tracheal fistula of a tracheotomized patient (from Loewy and von Schroetter).

lobe or an entire lung is occluded, the equilibrium is established much more rapidly. This may have some bearing on the observations of Van Allen, Lindskog and Richter, that if a tertiary bronchus is obstructed air will penetrate the obstructed portion of the lung from the surrounding alveoli, through what they describe as "alveolar pores." We shall discuss this point later. Loewy and von Schroetter said, however, that the decrease or oxygen in the circulating blood following the occlusion of an important portion of the respiratory area, with unhampered circulation, speeds up the passage of the alveolar oxygen into the capillary blood because of the increased differences in their

respective partial pressures. It is interesting to note here that Loewy and von Schroetter in this experimental work had already stated: 1. Prolonged obstruction will necessarily lead to atelectasis by complete absorption of the alveolar air. 2. During this process of absorption the intra-alveolar pressure in the occluded lung remains within normal limits. They explained this fact in the following way. The arterial blood will be polluted by its mixture with unaerated blood coming from the obstructed lung; the percentage of carbon dioxide will rise and oxygen decrease proportionally to the area of the obstructed pulmonary segment. In order to expel the excess of carbon dioxide the healthy lung is proportionally hyperventilated. This is effected by deepening of the respirations much more than by the increase in respiratory rate. This increase in size of the healthy lung augments the effect of the elastic recoil of the obstructed alveoli in their process of collapse while the gases are being absorbed. This positive pressure, the value of which is regulated by the extent of the occluded pulmonary area, exactly neutralizes the "negative pull" which theoretically, at least, should be exerted on the shrinking alveoli of the obstructed lung. The data furnished by Loewy and von Schroetter were of great help to us, although we discovered this article when our work was already terminated; we reached similar conclusions and used a somewhat similar technic completely independent of these authors.

It is peculiar that with the rather extensive clinical and pathologic knowledge concerning atelectasis, and notwithstanding these valuable data available in the literature, none of the many investigators on atelectasis has put the mechanism of its production on a sound physiologic basis.

EXPERIMENTAL WORK

TECHNIC

In previous papers we showed that atelectasis can be constantly produced experimentally if a bronchus is obstructed in an air-tight manner. For this purpose we elaborated a specially constructed catheter with a one-way valve elastic balloon which was introduced by the bronchoscope in a chosen valve of the dog. This balloon, described elsewhere, can be inflated from the outside and then detached from its connection and left in place. Roentgenographic examination of the animal placed on a special stand for obtaining symmetrical pictures shows the characteristic pictures of atelectasis with the displacement of the heart, the trachea and the diaphragm to the affected side, and opacity of the affected lung. We believe that if we were able to produce atelectasis regularly it was because we used as an obstructive agent an elastic balloon and not a solid plug of cork, wood or metal, such as that tried by others before and after our investigations. We are convinced that a solid body cannot com-

pletely obstruct a bronchus which yields and the diameter of which changes constantly with expiration and inspiration.[2]

The solution of our present problem, however, required a new technic. We had to devise an instrument that would enable us to obstruct completely a bronchus through the bronchoscope—in order to avoid opening of the chest or trachea. We must also be able to draw alveolar air from below the obstruction for determination of gas percentages and intrapulmonary pressure. After a number of trials we constructed the following two types of apparatus, which gave us full satisfaction.

Intrabronchial Cannulas.—The first apparatus is composed of two thin-walled brass tubes of 1 and 2 mm. internal diameter, respectively, and 50 cm. long. The external diameter of both tubes soldered together does not exceed from 6 to 7 mm., so that the instrument easily passes through Jackson's full lumen 9 mm. bronchoscope. The narrow tube terminates 15 mm. proximal to the larger one,

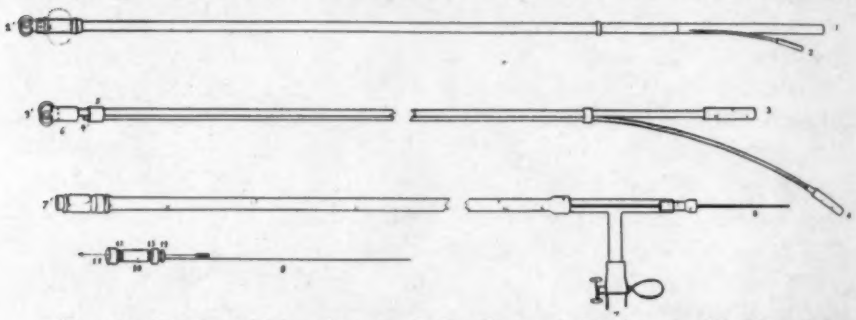

Fig. 5.—Intrabronchial catheters of Coryllos and Birnbaum. Model *1-1'* is composed of a large external metal tube (5 mm. in diameter) which terminates in a free end surrounded by a crown (*1'*) in order to avoid closure of this end by bronchial mucosa. A smaller tube passes into this tube and emerges 15 mm. from its distal end *1'*, where this tube is soldered, so that there is no connection between tubes 1 and 2. Around the distal end of the small tube is tied a piece of rubber tube, so that when air or fluid is introduced through *2* the rubber is distended, forming an obstructing balloon, as outlined. *3-3'* is the model described in the text, showing *3-3'* the larger, bronchial tube and *4-4'* the smaller one which serves for the inflation of the obstructing balloon which is not depicted in the picture. *7-8* is the latest model; it is more detailed but is not essentially different from the preceding ones.

which is longer and has around its free end a wire crown to avoid obstruction by bronchial mucosa. For the same reason small lateral openings are made around this end. Above and below the distal opening of the small tube, two brass rings are soldered around it, each of them bearing a groove for tying the small rubber balloon. Several models with more or less important modifications were made. In figure 5 *1'-1* shows a bronchial catheter in which the small brass tube passes inside the larger tube throughout its length and emerges near its distal

2. The ingenious tracheal cannula described by Van Allen and co-workers does produce a complete bronchial obstruction if well manipulated.

end, where it is filed down level with the outside tube, to which it is carefully soldered. Models 7 and 11 are the latest modification. A piece of fine india rubber tube (the tubing used for Kolman's urethral dilator is excellent) is put over the distal end of the cannula and securely tied around the groove with fine silk thread. This rubber tube is inflated through the small metal tube after the instrument is introduced into the chosen bronchus and forms an obstructing balloon. The accurate inflation of the balloon is one of the most important points of the technic. It must be sufficient to obstruct the bronchus completely, but not so excessive as to interfere with the circulation and innervation of the bronchus or with the ventilation of the other bronchi by displacement of the interbronchial spur or carina. These requirements are imperative, since as a rule these experi-

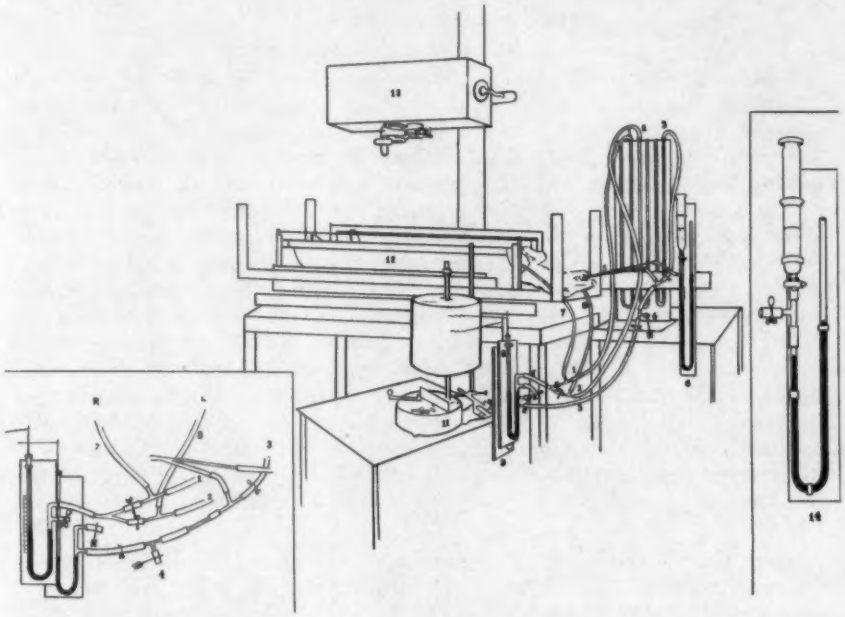

Fig. 6.—Lay-out of closed chest experiment. The animal is placed in our special x-ray stand (*12*) and the bronchus blocked by means of the intrabronchial catheter (*5*) connected to the mercury manometer *6*, (enclosure *14*) which allows checking up its degree of inflation. In each pleural cavity a cannula is placed connected to rubber tubes *7* and *8*. These tubes are connected (left enclosure) by T tubes to water manometers (*1* and *2*) and through another tube to a recording mercury manometer, so that it is possible to record on the smoked drum the tracing of the right or left pleural cavity pressures. The large bronchial tube of the bronchial catheter is connected by a T tube to a water manometer (*3*) and to a mercury manometer recording on the same smoked drum (*11*). A T tube was interposed into the latter rubber tube (*4*, left enclosure) allowing the taking of air specimens of intrapulmonary air for gas analysis.

ments last for many hours. It is necessary to know at all times whether the degree of inflation and obstruction remains unchanged. For this reason we devised a closed mercury manometer system (fig. 6, *14*) the free end of which was connected by

way of a T tube to a syringe of 30 cc. capacity. The horizontal tube was connected through a rubber tube to the small tube of the bronchial catheter. By pushing down the plunger of the syringe, already filled with water, we could inflate the balloon to a size a little greater than the estimated diameter of the bronchus on which bronchoscopy had previously been done, and a marker was placed at the height of the mercury meniscus in the closed end of the manometer. The bronchial catheter would then be disconnected. After it was introduced through the bronchoscope into the chosen bronchus, it would again be connected with the manometer and the plunger of the syringe pushed in to distend the balloon and bring the mercury meniscus slightly above the previously placed marker. As long as the mercury stood at this level we were certain that the balloon was inflated.

Two types of experiments were carried out.

Closed Chest Experiment.—In the first group, which will be designated by "closed chest experiment" (fig. 6), the animal, under iso-amyl-ethyl barbituric anesthesia, was placed on the x-ray stand (*12*) so that the evolution of the experiment could be watched by fluoroscopy and roentgen-ray pictures. The intrapleural pressures during the experiment were taken by two water manometers (*1, 2*) connected with two cannulas introduced into the pleural cavities of the animal. Through the bronchoscope the pulmonary cannula was introduced and the balloon inflated, as already described. The larger tube of the bronchial catheter, which communicated with the entrapped pulmonary air, was connected to a water manometer (*3*), to a recording mercury manometer and at times through a T tube (*4*) to the sampling bulb for analysis of specimens of alveolar air. In this way it has been possible to follow simultaneously the intrapleural pressures and to record them on a smoked drum (*11*), to read and record the intrapulmonary pressure in the obstructed lung, to follow the changes in the percentage of the entrapped alveolar air and to check up by fluoroscopy and roentgenographic examination the progress of atelectasis. At the same time, the closed mercury manometer connected with the small tube of the intrabronchial catheter enables us to know exactly the degree of inflation of the obstructing balloon.

Open Chest Experiment.—The second type of experiment will be designated "open chest experiment." In this series the chest of the animal (under iso-amyl-ethyl barbituric acid anesthesia) was opened by mediosternal section while intratracheal insufflation was being given. After careful hemostasis, the chest was widely retracted by two Balfour self-retaining rectractors fixed to the edges of the wound by stitches passing through the intercostal spaces so as to avoid displacement. The animal was then carried to the oscillating vacuum box (fig. 7), a detailed description of which has been given in a previous paper. The head was passed through the rubber tissue cuff (*6*, upper right angle enclosure) and this was applied around the previously shaved and petrolatum-anointed neck of the animal by means of cotton bandage (*7*). Intratracheal insufflation through the bronchoscope was only interrupted for the few seconds necessary to pass the head of the animal through the rubber cuff. Then the glass cover was applied and secured to the box to make it completely air-tight. In the meantime, the rotating valve (*8*) was connected with the suction faucet (*10*) and the number of its revolutions per minute regulated to the respiratory rate of the animal as it was before opening of the chest. The intrapleural pressure was taken before operation and the oscillations of negative pressure in the box (indicated in the water manometer 9), were regulated so as to be equal to the intrapleural pressure of the

animal before opening of the chest. From now on the intratracheal insufflation must stop, and the animal will breathe with its chest wide open at the same rate and with the lungs under the same negative pressure as in the closed chest. Moisture and temperature inside of the box were kept as near normal as possible. Figure 8 is a photograph of the lay-out of the whole experiment. It has been repeatedly possible to keep the animal in fine condition in the box for from eight to fifteen hours. A small tube was provided for, through which saline solution could be given subcutaneously if necessary without disturbing the experiment.

We wish to point out that this box is based on a different principle from the differential pressure chamber of Sauerbruch. In the latter, only one pleural

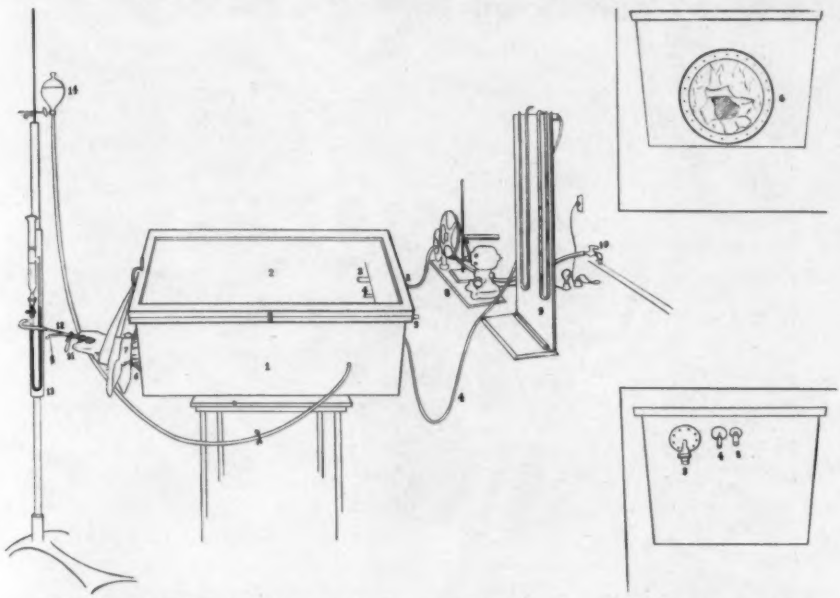

Fig. 7.—Lay-out of the open chest experiment in the oscillating vacuum box. After the chest is opened the animal is placed in the air-tight box (*1*) the cover of which (*2*) is made of plate glass. The head of the animal protrudes through the opening in the box, and the rubber tissue cuff attached around this opening (*6*, and upper left corner enclosure *6*) is fixed around the neck of the animal, previously shaved and anointed with petrolatum, by a bandage (*7*). The rotating valve (*8*), interspersed between the suction apparatus (*10*) and the box inlet (*3*) insures an oscillating vacuum in the box. This pressure is measured by the water manometer (*9*) and is equal to the negative intrapleural pressure of the animal taken previous to operation. Inlet *5* serves to regulate the pressure in the box. A rubber tube passes through one wall of the box and is connected to a reservoir with physiologic solution of sodium chloride; by this means fluids can be administered under the skin or into the peritoneum of the animal during the experiment. Through the bronchoscope (*11*) the bronchial cannula is introduced into the left stem bronchus, and the balloon which is to occlude the bronchus is then inflated by means of the syringe-mercury manometer arrangement described in figure 6. The large tube of the cannula, in communication with the entrapped intrapulmonary air, is closed off unless samples of air are to be withdrawn through it for gas analysis.

cavity being open, the steady and nonoscillating differential pressure (hypo or hyper) serves to keep the lung of the opened half-chest distended while the other lung breathes normally. In our box, on the contrary, both pleural cavities being widely opened, no respiration can take place unless there is an oscillation in the negative pressure box.

EXPERIMENTAL MATERIAL AND PURPOSE OF INVESTIGATION

The experiments were carried out exclusively on dogs, from 10 to 20 Kg. in weight, because of the relatively large diameter of their tracheae and bronchi, which allow easy intrabronchial manipulation.

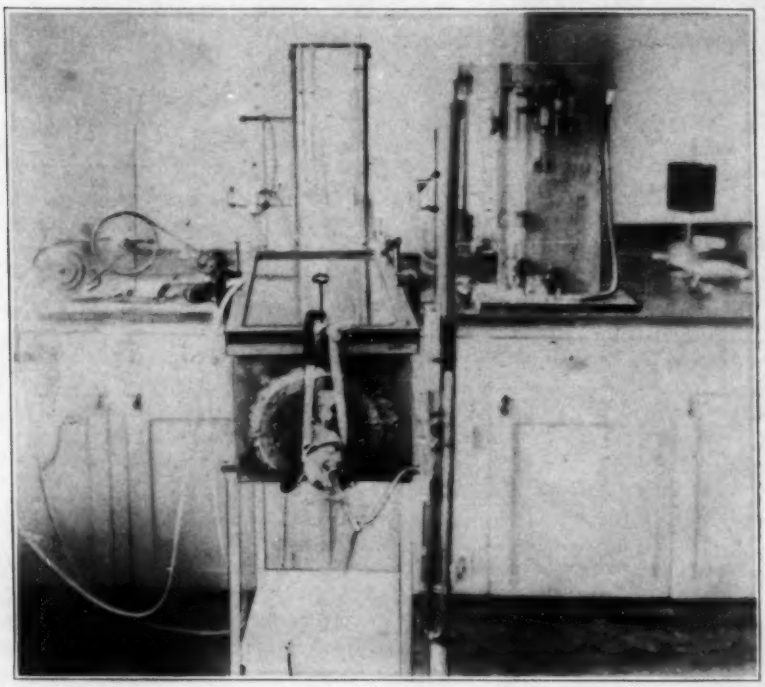

Fig. 8.—Open chest experiment series. Photographic view of the lay-out.

Forty-seven animals were used for this experimental investigation. They were anesthetized by the intraperitoneal injection of 10 per cent solution of iso-amyl-ethyl barbituric acid, 55 mg. per kilogram of body weight being given with additional smaller doses after from five to six hours; thus prolonged anesthesia was made possible. Two animals died from the anesthetic. The others withstood the anesthetic well for the long duration of the experiment.

In this work the points investigated were the following:

(1) The fate of the alveolar air entrapped in a pulmonary lobe after complete occlusion of the corresponding bronchus

(2) The changes produced in the entrapped alveolar air as indicated by successive gas analyses

(3) Whether entrapped air is absorbed and at what rate

(4) The speed of absorption of the different gases composing the alveolar air (oxygen, carbon dioxide) when introduced individually into the lung of the living animal, previously rendered atelectatic, and what gas exchanges take place thereafter

(5) What happens when neutral gases are introduced separately into the atelectatic lung (nitrogen, hydrogen and helium)

(6) How the respiratory membrane behaves toward anesthetic gases or vapors (nitrous oxide, ethylene, ethyl-chloride, ether vapor)

(7) The changes, if any, in the intrapulmonary pressure during the process of gas absorption.

The results obtained in successful experiments have been uniform, with small differences within limits of experimental error, inevitable with experiments so complicated and of such long duration. Before examining each of the foregoing questions separately, the protocols of four experiments will be given, two of the first type (closed chest) and two of the second type (open chest). Each of them is representative of the respective type.

ABSORPTION OF OXYGEN AND CARBON DIOXIDE

Closed Chest Experiment (dog 489).—The experiment lasted nine and a half hours.

May 5, 1930: 11:45 p. m.: The rubber balloon on the cannula was introduced into the right lower bronchus.

11:52 p. m.: The balloon was blown up with 3 cc. of water.

11:54 p. m.: A sample of gas was obtained from the obstructed lung, 15 cc.; it contained 5.85 per cent carbon dioxide and 9.05 per cent oxygen.

12:03 p. m.: A sample of gas contained 5.98 per cent carbon dioxide and 6.66 per cent oxygen.

12:17 p. m.: A sample of gas contained 5.9 per cent carbon dioxide and 6.43 per cent oxygen.

12:28 p. m.: A sample of gas contained 6.1 per cent carbon dioxide and 7.36 per cent oxygen.

12:41 p. m.: A sample of gas contained 6.07 per cent carbon dioxide and 6.15 per cent oxygen.

12:52 p. m.: A sample of gas contained 6.05 per cent carbon dioxide and 6.02 per cent oxygen.

1:21 a. m.: Only 2 cc. of gas could be obtained.

1:35 a. m.: A roentgenogram showed a definite shift of the heart to the right.

1:53 a. m.: One hundred cubic centimeters of oxygen was introduced into the obstructed lung. Roentgenograms taken one and two minutes later showed the heart shifted to the left.

1:58 a. m.: A sample of gas from the obstructed lung contained 6.94 per cent carbon dioxide and 51.2 per cent oxygen.

2:10 a. m.: A roentgenogram showed the heart again back to the right side

2:15 a. m.: Only 4 cc. of gas could be obtained; this amount was insufficient for analysis.

2:22 a. m.: Fluoroscopy showed the heart a little more to the right than before the administration of oxygen. The respiration was very quiet.

3:50 a. m.: Fluoroscopy showed increased density of the right lower lobe.

5:26 a. m.: One hundred cubic centimeters of carbon dioxide was introduced into the obstructed lung.

5:26½ a. m.: The heart was shifted to the left; the right lower lobe was clear.

5:30 a. m.: Only 4.8 cc. of gas could be obtained. It contained 54.16 per cent carbon dioxide.

5:32 a. m.: A roentgenogram showed the heart back again on the right; the breathing was very quiet.

6:25 a. m.: Fluoroscopy showed no further change; the right side of the diaphragm was immobile, and the heart moved toward the right on inspiration. There was no ventilation in the obstructed lung.

9:15 a. m.: A roentgenogram showed no change. The animal was killed with 30 cc. saturated solution of magnesium sulphate injected intravenously.

9:20 a. m.: Autopsy revealed atelectasis of the right lower and accessory lobes (confirmed by microscopic sections).

Open Chest Experiment (dog 498).—The experiment lasted fourteen hours; negative pressure was —4, —7.5 of water; oscillation rate, 14 per minute.

May 15, 1930: 11:35 a. m.: The left lung was obstructed.

1:07 p. m.: A sample of gas contained 6.09 per cent carbon dioxide and 4.74 per cent oxygen.

8:30 p. m.: Atelectasis was complete in nine hours.

10:40 p. m.: One hundred cubic centimeters of oxygen was introduced to distend the left lower lobe.

10:50 p. m.: A sample of gas contained 8.59 per cent carbon dioxide; the oxygen percentage was beyond the limit of the apparatus..

11:00 p. m.: The left lower lobe was again atelectatic; all the gas was absorbed.

11:10 p. m.: One hundred cubic centimeters of oxygen was introduced to distend the left lower lobe.

11:20 p. m.: The left lower lobe was again atelectatic; all gas was absorbed.

11:25 p. m.: One hundred cubic centimeters of oxygen was introduced to distend the left lower lobe.

11:31 p. m.: The left lower lobe was much smaller; 100 cc. more of oxygen was introduced.

11:35 p. m.: A sample of gas contained 10.63 per cent carbon dioxide; the oxygen percentage was beyond the limit of the apparatus.

12:13 a. m.: One hundred cubic centimeters of carbon dioxide was introduced to distend the left lower lobe.

12:14½ a. m.: All the carbon dioxide was absorbed; the lobe was again atelectatic.

12:16 a. m.: One hundred cubic centimeters of oxygen was introduced to distend the left lower lobe again.

12:27 a. m.: The oxygen was completely absorbed; the lower left lobe was again atelectatic.

12:37 a. m.: Fifty cubic centimeters of oxygen and 50 cc. of carbon dioxide was introduced to distend the lower left lobe.

12:38 a. m.: A sample of gas contained 30 per cent of carbon dioxide; the sample was insufficient for oxygen analysis.

12:41 a. m.: All the gas was absorbed; the lobe was again atelectatic.

1:02 a. m.: One hundred and fifty cubic centimeters of 100 per cent ether vapor was introduced to distend the lower lobe.

1:03 a. m.: All the ether was absorbed; the lobe was atelectatic again.

1:09 a. m.: One hundred cubic centimeters of nitrogen was introduced into the left lower lobe.

1:25 a. m.: The heart stopped beating; the lung was unchanged.

Summary: The absorption time for oxygen averaged 15 minutes; for carbon dioxide, 1.5 minutes; for equal parts of carbon dioxide and oxygen, 4 minutes; for 100 per cent ether vapor, 1 minute.

ABSORPTION OF VARIOUS GASES BY THE LUNG

Closed Chest Experiment (dog 511).—The dog weighed 22 Kg. Fluoroscopic and roentgenographic control was employed.

May 23, 1930: 2:00 p. m.: Iso-amyl-ethyl barbituric acid, 60 mg. per kilogram of body weight, was used. The animal was asleep at 2:14 p. m.

3:45 p. m.: The animal was placed on the stand; a double bronchial cannula was introduced, and the left lung obstructed by inflation of the balloon.

4:30 p. m.: The left lung was irrigated with oxygen. It appears that the side of the cannula was obstructing the left upper lobe and the balloon the left lower lobe, but the obstruction did not seem complete because on aspiration of the cannula the lung did not appear to decrease in size under fluoroscopy.

5:30 p. m.: The left lung was again blocked and irrigated seven times with oxygen.

5:35 p. m.: In the first roentgenogram the oxygen was shown to be absorbing.

6:30 p. m.: A second roentgenogram was taken.

7:05 p. m.: Oxygen, 275 cc., was introduced into the left lung by means of the pneumothorax apparatus which registered an intrabronchial pressure of from + 1 to 2 during the introduction. A third roentgenogram was made (fig. 9 *A*).

7:20 p. m.: A fourth roentgenogram showed complete absorption of oxygen in the left lower lobe (fig. 9 *B*).

7:35 p. m.: No further change was noted; 225 cc. of oxygen was again introduced. A roentgenogram was made.

7:52 p. m.: Fluoroscopy showed complete absorption of gas.

8:00 p. m.: Carbon dioxide, 290 cc., was introduced (fig. 10 *A*).

8:05 p. m.: Fluoroscopy showed complete absorption of gas.

8:10 p. m.: A roentgenogram confirmed the fluoroscopic observation.

8.30 p. m.: Fluoroscopy showed perhaps a slightly greater absorption than at 8:10.

8:47 p. m.: Nitrous oxide, 280 cc., was introduced into the left lower lobe (fig. 11 *A*).

8:58 p. m.: The roentgenogram showed practically complete absorption of the gas (fig. 11 *B*). With a syringe, 5 cc. of serous fluid and 2 cc. of frothy material was aspirated from the left lower lobe. This is the first time fluid has been noticed.

9:05 p. m.: Seven cubic centimeters of slightly frothy fluid was aspirated from the left lower lobe.

9:10 p. m.: One cubic centimeter of fluid was aspirated. Fluoroscopy showed no further absorption of nitrous oxide.

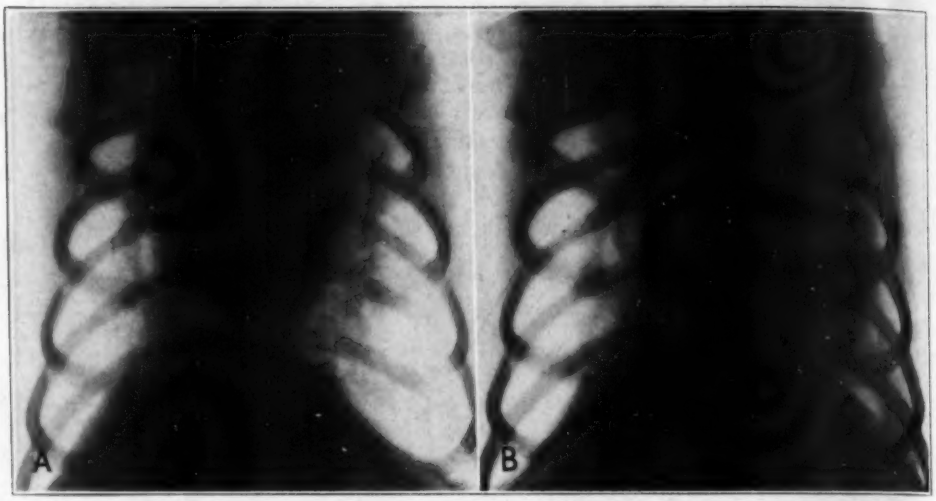

Fig. 9 (dog 511).—*A* was taken after the introduction of 275 cc. into the left lower lobe which appears distended; *B*, fifteen minutes after the introduction of 275 cc. of oxygen into the lower left lobe. The gas has been completely absorbed. The clear area at the base of the left lung is due to an abnormal position of the accessory (right) lobe, as proved by autopsy. See figure 15.

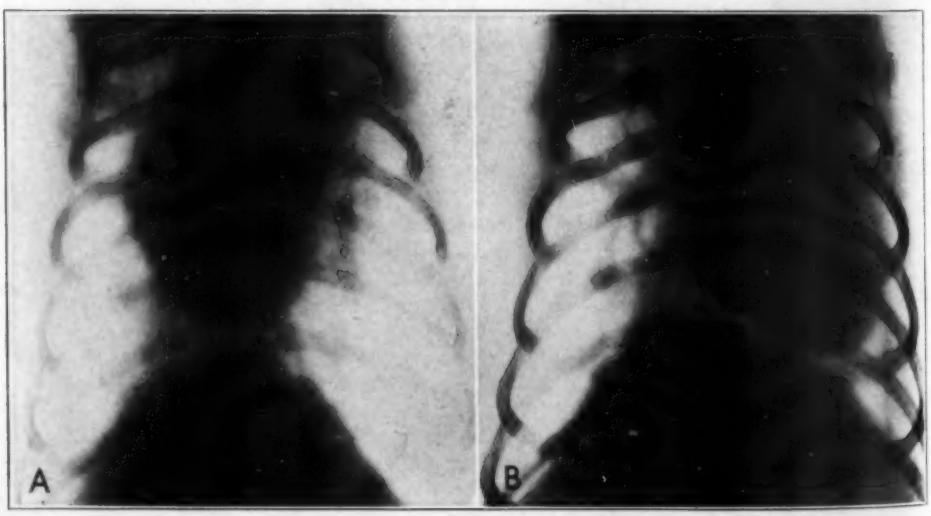

Fig. 10 (dog 511).—*A* was taken after the introduction of 290 cc. of carbon dioxide into the left lower lobe which appears distended; *B*, ten minutes after the introduction of carbon dioxide into the left lower lobe. The gas has been completely absorbed.

9:25 p. m.: Roentgenogram showed that nitrous oxide had been absorbed. Three cubic centimeters of frothy fluid was extracted from the left lower lobe.

9:40 p. m.: Oxygen, 275 cc., was introduced into the left lower lobe, and a roentgenogram made.

9:55: Oxygen was absorbed, as shown by fluoroscopy.

10:10 p. m.: Two hundred and fifty cubic centimeters of ethylene was introduced (fig. 12*A*).

10:22 p. m.: Fluoroscopy showed practically complete absorption.

11:35 p. m.: Seven cubic centimeters of free gas and 24 cc. of serous fluid were extracted from the left lung by a syringe. A roentgenogram showed no further change (fig. 12*B*).

May 24, 12:30 a. m.: Three and a half cubic centimeters of iso-amyl-ethyl barbituric acid was given peritoneally. Fluoroscopy showed no further change.

6:30 a. m.: One and one half cubic centimeters of mucoserous fluid was removed from the left lung, and a roentgenogram made.

7:10 a. m.: Oxygen 280 cc., was introduced into the left lung.

7:20 a. m.: About 2 cc. of free gas could be withdrawn through the bronchial cannula from the left lower lobe.

7:24 a. m.: Fluoroscopy showed the absorption of oxygen to be complete.

7:25 a. m.: Carbon dioxide, 275 cc., was introduced into the left lung.

7:30 a. m.: The absorption of carbon dioxide was complete; no serum.

7:35 a. m.: Etheylene, 275 cc., was introduced into the left lung.

7:47 a. m.: Seventeen cubic centimeters only of free gas could be withdrawn with a syringe from the left lower lobe, which was again injected in the lung.

8:20 a. m.: Fifteen cubic centimeters of free gas could be withdrawn from the left lung; this gas was returned to the lung as in former instances. No fluid could be withdrawn. A roentgenogram was made. This was no different than ten minutes after introduction of ethylene. The great mass of the gas was absorbed rapidly, the rest taking a long time.

9:15 a. m.: There was still 15 cc. of free gas that could be withdrawn from the left lower lobe; 12 cc. was returned to the lung. The gas in the syringe smelled like ethylene.

9:40 a. m.: Twelve cubic centimeters of gas could still be withdrawn easily.

10:00 a. m.: Ten cubic centimeters of gas could still be withdrawn easily; this was not returned to the lung. Four cubic centimeters of iso-amyl-ethyl barbituric acid was given peritoneally.

1:40 p. m.: Oxygen, 275 cc., was introduced into the left lower lobe

1:52 p. m.: The absorption of oxygen was complete as seen by fluoroscopy; no fluid could be aspirated.

1:54 p. m.: Carbon dioxide, 250 cc., was introduced into the left lower lobe.

1:57 p. m.: Absorption seemed complete by fluoroscopy; no fluid could be withdrawn.

2:08 p. m.: Nitrous oxide (water washed), 250 cc., was introduced into the left lung.

2:12 p. m.: Only thirteen cubic centimeters of free gas could be withdrawn; it was returned to the lung.

2:15 p. m.: Eleven cubic centimeters of free gas could be withdrawn; it was returned to the lung.

2:20 p. m.: Ten cubic centimeters of free gas could be withdrawn; this 10 cc. was rejected; there was no serum or fluid.

2:25 p. m.: No fluid or mucus could be withdrawn.

2:26 p. m.: Nitrous oxide (dry), 250 cc., was introduced into the left lung.

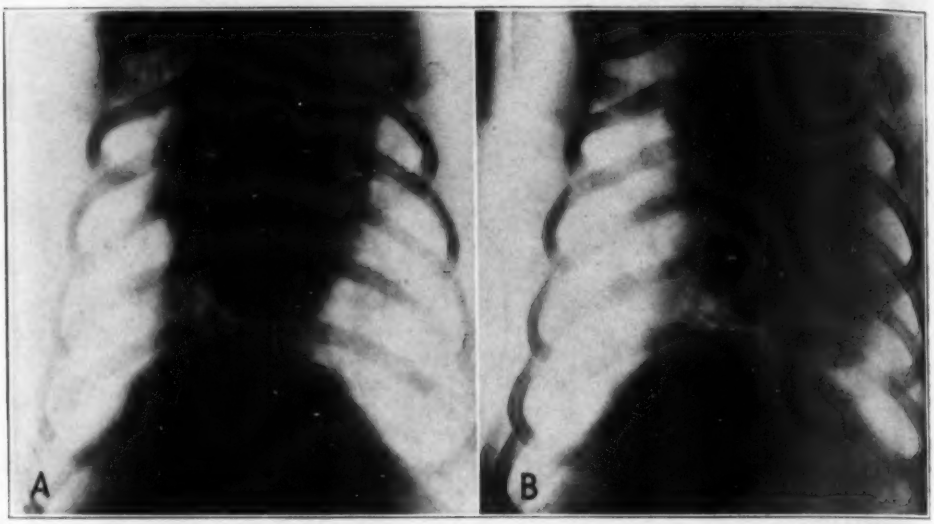

Fig. 11 (dog 511).—*A* was taken after the introduction of 280 cc. of nitrous oxide into the left lower lobe; *B*, eleven minutes after the introduction of 280 cc. of nitrous oxide. The gas has been absorbed.

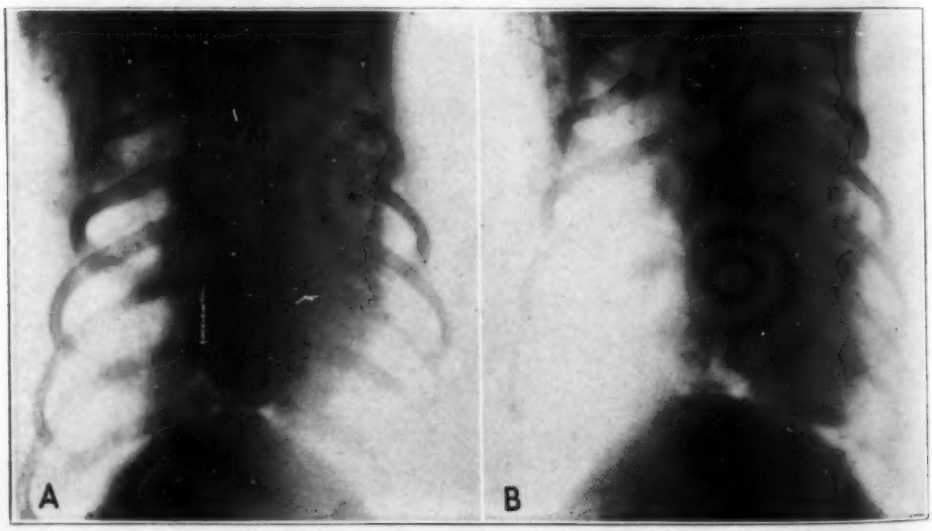

Fig. 12 (dog 511).—*A* was taken after the introduction of 250 cc. of ethylene into the left lower lobe; *B*, after the absorption of ethylene.

2:30 p. m.: Fourteen cubic centimeters of free gas could be withdrawn; it was returned to the lung.

2:33 p. m.: Eleven cubic centimeters of free gas could be withdrawn; it was returned to the lung.

2:39 p. m.: Nine and one-half cubic centimeters of free gas could be withdrawn; it was returned to the lung.

2:48 p. m.: Nine cubic centimeters of free gas was withdrawn from the lung and rejected; no fluid or mucus was found.

2:52 p. m.: The left lung was irrigated three times with oxygen.

2:57 p. m.: Absorption seemed complete by fluoroscopy; no fluid could be withdrawn.

3:17 p. m.: Nitrous oxide, 20 cc., was introduced into the left lower lobe.

3:18 p. m.: Twelve cubic centimeters of free gas could be withdrawn; it was returned to the lung.

3:19 p. m.: Seven cubic centimeters of free gas could be withdrawn; it was returned to the lung.

3:20 p. m.: Four cubic centimeters of free gas could be withdrawn; it was returned to the lung.

3:22 p. m.: Three cubic centimeters of free gas could be withdrawn; it was returned to the lung.

5:50 p. m.: The absorption of gas seemed complete by fluoroscopy. A mixture of equal parts of helium and oxygen, 200 cc., was introduced into the left lower lobe, and a roentgenogram made.

7:20 p. m.: A roentgenogram showed partial absorption of gas.

8:00 p. m.: Analysis of the gas showed 5.86 per cent oxygen, and 8.29 per cent carbon dioxide. The remainder of the free gas, in the lung, 116 cc., was aspirated. No fluid or mucus was found. Fluoroscopy showed the lung to be collapsed.

8:08 p. m.: One-half cubic centimeter of mucus was aspirated.

8:10 p. m.: A roentgenogram was made.

8:30 p. m.: The left lower lobe was irrigated three times with helium and then 175 cc. of helium (pure water-washed) was introduced into the left lower lung. Fluoroscopy showed the lower lobe to be distended.

9:15 p. m.: By fluoroscopy, the left lower lobe seemed slightly increased in size.

9:20 p. m.: Twenty cubic centimeters of gas was withdrawn from the lung for analysis, which showed 5.83 per cent oxygen and 9.34 per cent carbon dioxide.

10:30 p. m.: There was no apparent change in the lung.

12:00 p. m.: There was no apparent change in the lung.

May 25, 1:00 a. m.: Thirty-five cubic centimeters of gas was withdrawn from lung for analysis, which showed 5.34 per cent oxygen and 6.22 per cent carbon dioxide.

1:10 a. m.: One hundred and forty cubic centimeters of gas was withdrawn, leaving 15 cc. of available gas in the lung. Fluoroscopy showed the left lower lobe almost totally collapsed.

2:00 a. m.: The last 18 cc. of available gas was withdrawn for analysis, which showed 5.25 per cent oxygen and 6.64 per cent carbon dioxide.

2:10 a. m.: The lung was irrigated five times with oxygen.

2:15 a. m.: No free gas or fluid could be aspirated. Fluoroscopy showed complete collapse.

2:20 a. m.: Two and one-half cubic centimeters of iso-amyl-ethyl barbituric acid was administered.

3:30 a. m.: Eighty cubic centimeters of physiologic solution of sodium chloride was given subcutaneously.

9:10 a. m.: Fourteen and one-half cubic centimeters of iso-amyl-ethyl barbituric acid was given. The dog breathed quietly.

11:00 a. m.: A roentgenogram was made.

12:25 p. m.: A roentgenogram was made.

12:30 p. m.: The animal was killed by intravenous injection of 10 cc. of a saturated solution of magnesium sulphate.

Post Mortem: The left upper lobe was completely atelectatic. The left lower lobe was completely atelectatic and moderately edematous (fig. 13).

Open Chest Experiment (dog 504).—The dog weighed 12 Kg.

May 17, 1930, 10:30 a. m.: Iso-amyl-ethyl barbituric acid, 60 mg. per kilogram of body weight, was given.

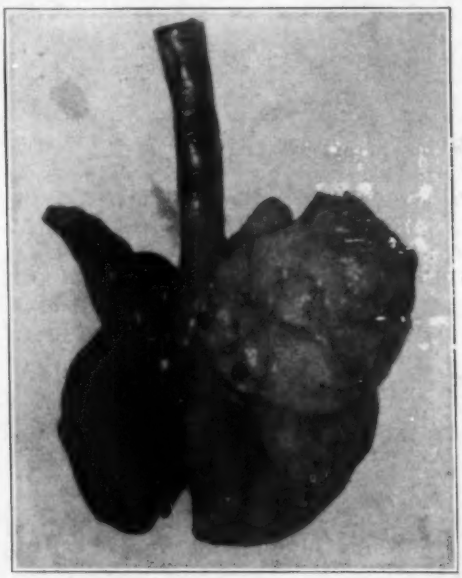

Fig. 13 (dog 511).—Posterior view of the (left, atelectatic) lung extracted from the chest.

11:55 a. m.: Ephedrine sulphate, one-half grain (0.32 mg.) was given subcutaneously; the respiratory rate was 16; the pulse rate 140.

12:00 a. m.: The animal was placed in the vacuum box; the respiratory rate was 12, the pulse rate 145.

12:37 p. m.: The left lung was obstructed, had been washed out six times with oxygen and left inflated with oxygen.

1:40 p. m.: Atelectasis was progressing slowly. The lung was rewashed once with oxygen.

1:52 p. m.: The bronchial cannula was withdrawn.

1:58 p. m.: The cannula was reintroduced and the balloon inflated.

2:00 p. m.: The whole left lung was aspirated seven times, and oxygen introduced each time. The lung was then aspirated and left in the collapsed state.

2:15 p. m.: The respiratory rate was 10, the pulse rate 128. The manometer excursion (one-half the actual value) was —2 to —7 cm. of water.

2:33 p. m.: A long glass tube was connected to the bronchial catheter and allowed to dip down into a large beaker of water which was placed 2 feet (60.91 cm.) below the level of the catheter. It was noticed that on inspiration water was sucked up to a height of 8 cm., and on expiration the height of the column went down to 6 cm.

2:50 p. m.: Nitrous oxide was introduced from a tank into a large leveling bulb, immersed under water, to wash out the air and fill it with the gas. It was then disconnected from the tank and its outlet connected to the obstructed lung. In this way 175 cc. of the gas was introduced over a period of four minutes.

3:05 p. m.: The respiratory rate was 12, the pulse rate 168 (spontaneous respiration, five per minute).

3:17 p. m.: There were rapid respiratory movements independent of the manometer excursion. Two cubic centimeters more of iso-amyl-ethyl barbituric acid, one-fourth grain (16 mg.) of morphine and 2 mg. of atropine was given subcutaneously.

3:25 p. m.: The lower lobe was almost entirely blue; the upper lobe was slightly so. The temperature was 40 C. (104 F.).

3:30 p. m.: The lower lobe was atelectatic. The upper lobe was further advanced but not completely airless.

3:35 p. m.: The lower lobe was completely atelectatic.

3:36 p. m.: The temperature in the box was 34 C.

3:38 p. m.: The upper lobe was completely atelectatic except for a small portion at the hilus and a small part of the periphery.

3:45 p. m.: Carbon dioxide (175 cc.) was introduced into the left lung to distend it to the same size it was with nitrous oxide (175 cc.).

3:47 p. m.: The gas was absorbing rapidly.

3:53 p. m.: There was a diffuse patchy involvement over the entire surface of both left lobes.

4:02 p. m.: Atelectasis was complete in both lobes of the left lung.

4:04 p. m.: Ethyl chloride vapor was introduced directly into the left lung; introduction was complete at 4:04½.

4:06 p. m.: Atelectasis progressed rapidly.

4:10 p. m.: The pulse rate was 172, the respiratory rate 12; the spontaneous respiratory movement was 56.

4:14 p. m.: Atelectasis was complete.

4:16 p. m.: Ethylene (175 cc.) was introduced directly into the left lung.

4:27 p. m.: Absorption was going on slowly; reflexes were present.

4:45 p. m.: Atelectasis was complete in the lower lobe except at the periphery. In the upper lobe, atelectasis was beginning in the midportion of the lung.

4:48 p. m.: Both lobes were about the same as before; the pulse rate was 180, respiratory rate 12 and spontaneous respiration 56 and irregular. The manometer excursion was —2 to —7 on one half of the manometer limb.

5:15 p. m.: Atelectasis was still progressing slowly. The tip of the upper lobe and the periphery were still expanded.

5:21 p. m.: Atelectasis was progressing definitely but slowly; reflexes were present.

5:29 p. m.: Atelectasis was complete.

5:31 p. m.: Carbon dioxide (200 cc.) was introduced into the left lung over a period of forty-five seconds to distend it completely. The tip of the upper portion of the upper lobe had become dry and adherent to the mediastinum.

5:35 p. m.: Absorption was going on rapidly.

5:43 p. m.: Atelectasis was complete in the lower lobe. It had progressed further in the lower part of the upper lobe than in the upper part of the upper lobe.

5:52 p. m.: Atelectasis was complete.

5:53 p. m.: Ethyl chloride (500 cc.) was again introduced into the left lung over a period of two minutes. It appeared that absorption was going on as fast as the gas was introduced. It was difficult to inflate the lung.

5:55 p. m.: The animal was deeply cyanotic; the pulse rate was 180; the pupils were dilated, and the reflexes were absent.

5:59 p. m.: Absorption progressed rapidly.

6:05 p. m.: The eye reflex had returned; cyanosis had disappeared.

6:10 p. m.: The rate of absorption was definitely slower. The lower lobe was practically completely atelectatic. The upper lobe, especially the upper portion, was still slightly expanded.

6:15 p. m.: The pulse rate was 168; the manometric respiration, 14; spontaneous respiration, 48. The manometer excursion was —3.5 to —8.5 cm. of water.

6:30 p. m.: Atelectasis was complete except in portions of the upper part of the upper lobe.

6:39 p. m.: Atelectasis was complete except at the periphery of the upper part of the upper lobe.

6:45 p. m.: Atelectasis was complete.

6:48 p. m.: Carbon dioxide (300 cc.) again was introduced over a period of thirty seconds.

6:59 p. m.: Absorption thus far had been fairly rapid. There was no definite area of atelectasis yet visible.

7:05 p. m.: Absorption was progressing somewhat slower.

7:15 p. m.: The lower lobe and a large portion of the lower part of the upper lobe were atelectatic.

7:20 p. m.: The pulse rate was 168; manometric respiration, 18; spontaneous respiration, 18. The manometric excursion was —2.5 to —7 cm. of water.

7:30 p. m.: Atelectasis was complete in the lower lobe. The upper lobe and tip of the lower half were expanded, especially at the periphery.

8:00 p. m.: Atelectasis was complete except for a strip at the center and the periphery of the upper portion of the upper lobe.

8:10 p. m.: Atelectasis was complete. The pulse rate was 176; manometric respiration, 18; spontaneous respiration, 20. Manometric oscillation was from —3 to —7 cm. of water.

8:12 p. m.: Ethylene (300 cc.) was introduced into the lung over a period of two minutes. The last portion of the lung to collapse was the first to expand.

8:25 p. m.: The lower lobe and lower portion of the upper lobe was almost completely atelectatic. The upper portion of the upper lobe showed patchy atelectasis.

8:40 p. m.: Atelectasis was complete except for a strip in the center of the upper lobe and scattered portions of the periphery of the upper lobe.

8:45 p. m.: Atelectasis was complete.

8:46 p. m.: Oxygen (300 cc.) was introduced into the left lung to expand it to previous size.

8:48-8:55 p. m.: The motor on the suction machine stopped. It was necessary to rotate the valve by hand till the motor was adjusted.

9:00 p. m.: Absorption of oxygen had progressed rapidly. Atelectasis was nearly complete except for the periphery of the upper part of the upper lobe.

9:04 p. m.: The pulse rate was 164, both the manometric and spontaneous respirations were 18. The manometric excursion was —4 to —8.5 cm. of water.

9:05 p. m.: Atelectasis was complete except for a few areas at the periphery of the upper part of the upper lobe.

9:07 p. m.: Atelectasis was complete.

9:13 p. m.: Ether vapor was introduced over a period of one minute and a half.

9:16 p. m.: The left lung collapsed but remained pink in color—not the liver-like appearance of atelectasis.

9:22 p. m.: Atelectatic areas were appearing in the lower lobe and lower portion of the upper lobe. Absorption was going on at a moderate rate. The animal was showing extreme cyanosis.

9:23 p. m.: The heart was very irregular.

9:25 p. m.: The animal died.

Post Mortem: The left upper lobe was completely atelectatic; the left lower lobe was edematous, friable and hemorrhagic.

Figures 14 *A* and *B* are histologic sections of the upper lobes in closed and open chest experiments showing complete atelectasis. Figure 15 showed interstitial hemorrhage and edema of the lung produced by the introduction of ether vapor into a lung previously rendered atelectatic.

PROBLEMS INVESTIGATED

I. *Fate of Alveolar Air Entrapped in a Pulmonary Lobe After Complete Occlusion of Corresponding Bronchus.*—In all our experimental animals atelectasis was produced within from six to fifteen hours. They were all under deep anesthesia so that the point raised by Van Allen and Adams, namely, that animals with a lobar or larger bronchus obstructed do not get atelectasis unless they are insufficiently anesthetized or have strained respiration, is not verified by our experiments. On the other hand, we believe that the assertion of these authors, that when a tertiary lobe is occluded atelectasis does not occur, is correct, but we do not agree entirely as to the explanation of this phenomenon given by them. They attribute it to the passage of air from the adjoining alveoli, through microscopic holes—the alveolar pores present in the interalveolar spaces. Such pores do really exist and were described long ago. A. Nicolas, in Poirier's textbook of anatomy (vol. 4, p. 528) said, "Is the homogeneous hyaline membrane, which with the respiratory epithelium constitutes the wall of the alveoli, normally perforated or not? It is generally conceded that in aged persons interalveolar perforations can be observed due to local resorption and atrophy of the respiratory membranes. The majority of authors (Shultz, Koelliker, Water, F. E. Shultze) deny the existence of these alveolar pores in normal persons. Others (Hauseman, F. Merkel) just as affirmatively argue their existence." Letulle (vol. 1, p. 13) does not admit their existence in normal lungs of young persons but believes they may exist in advanced age and calls them "trous d'usure." This

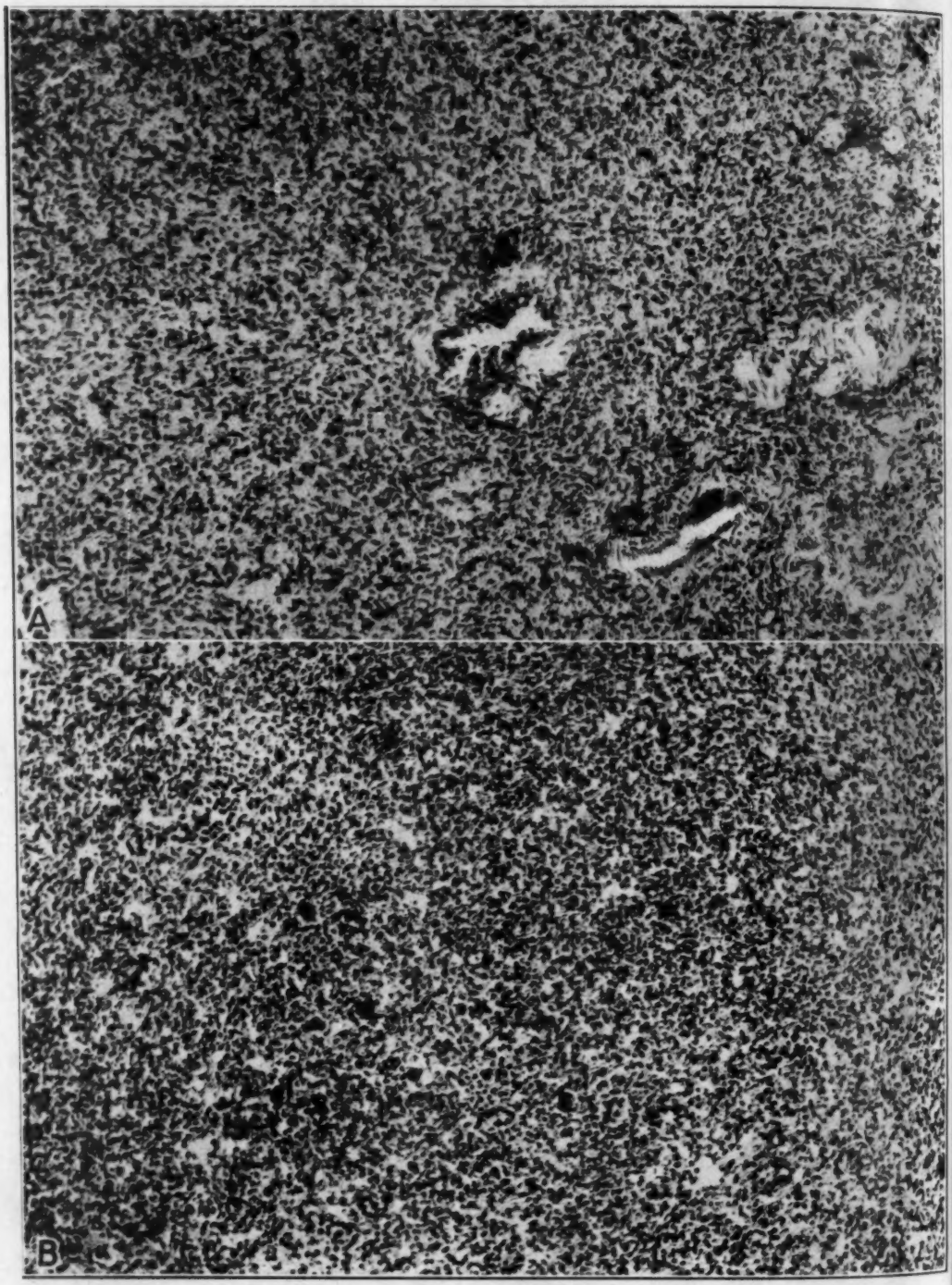

Fig. 14.—*A*, photomicrograph showing atelectasis produced in the closed chest experiment in a dog; *B*, atelectasis produced in the open chest experiment.

discussion brings to mind the discussion about the existence of similar pores in the mediastinum of the dog. This latter problem is solved today in favor of the nonexistence of anatomic pores permitting direct communication between the two pleural cavities; but the mediastinum of the dog is none the less readily permeable to air and even to fluids. The same reasoning applies to the extremely thin respiratory alveolar endothelium, and there is no necessity for real anatomic openings to explain the ready diffusion of air through the interalveolar septums. A definite experimental proof of this conception lies in the fact that

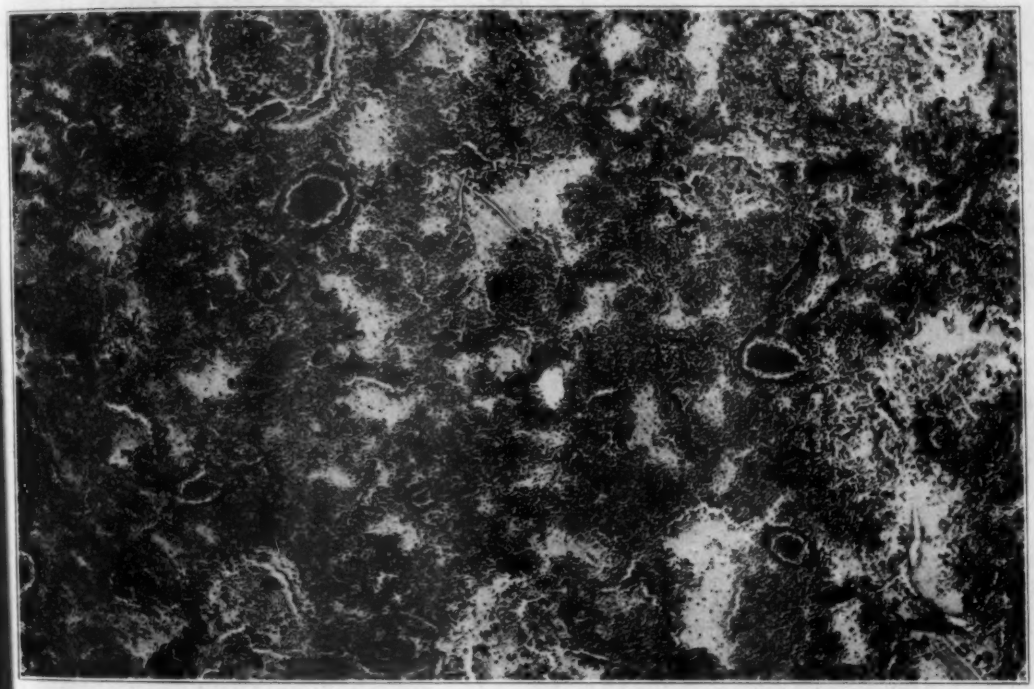

Fig. 15.—Interstitial hemorrhage and edema in the left lower lobe after introduction of 100 per cent ether vapor into the lung previously rendered atelectatic (open chest experiment).

whereas air comes out freely through the cannula obstructing a tertiary bronchus and continues to come out for hours, it will stop immediately if we introduce through the cannula a few cubic centimeters of 100 per cent ether vapor, which produces edema of the alveolar epithelium. This may show that patchy atelectasis cannot occur in a healthy lung; but just as soon as there is a slight inflammatory edema it is produced exactly in the same way as when a lobar bronchus is occluded. So much for bronchiolar obstruction.

Such a controversy does not exist when a lobar or common bronchus is obstructed. Atelectasis may require more or less time to be completed, but it inevitably occurs provided the lung circulation is normal and the alveolar endothelium not greatly altered. Increase in intrapulmonary pressure or a temporary one-way valve obstruction allowing air to be expired but not inspired, naturally does accelerate the completion of atelectasis. In the case of increased intrapulmonary pressure, this acceleration would occur because of increase in the total, and consequently of the partial, pressures of the alveolar gaseous components (see comment); in the second case it would occur, if such a mechanism is really possible in man, with the anatomic funnel-like configuration of the bronchial tree, because a portion of the alveolar air is mechanically eliminated, thus leaving less air to be absorbed. This is exactly what happened in the dogs of Van Allen and Adams when a portion of the air was allowed to be eliminated from the occluded lung. But in every case, when a big bronchus is occluded, atelectasis will follow. This statement is proved, in our own case, by many experiments on dogs, (over 400), with roentgenographic and postmortem control. Moreover, in the experiments with the open chest it is easy to follow up the production of atelectasis by direct vision and to produce it at will and at different speeds by varying quantitatively and qualitatively the composition of the alveolar gaseous content. If atelectasis is not produced after bronchial obstruction, this means that the obstruction is not complete. Of the completeness of the obstruction, there is but one real proof. This is the rapid decrease in the percentage of oxygen in the alveolar air. We think we may state that when within ten minutes after bronchial obstruction the oxygen in the alveolar air does not decrease from 15 or 16 per cent to about 6 per cent, there is not complete bronchial occlusion. This principle, if used as a criterion in every experimental work on atelectasis, will avoid the making of many unwarranted statements. Such being the case, apneumatosis (airlessness) always following complete bronchial obstruction, there is but one other way for the air to leave the lung, the venous alveolar blood. A positive proof of this will be given.

In the compressed lung as in open or tension pneumothorax, or when fluid is present in the pleural cavity, the mechanism of atelectasis, contrary to the prevailing opinion, is exactly the same. In fact, when the lung collapses the small bronchioli collapse at the same time, and their lumen is obstructed. Proof of this is that air is entrapped in the alveoli which will remain there, unless life, and with it, circulation, continue for a sufficient length of time. Lichtheim proved this fact in 1879. Collapsed lung is not synonymous with atelectatic or apneumatic (airless) lung, the difference between them being that alveolar air is present

in the former. How, then, would this air remain in the perfectly elastic alveoli if there were no bronchial obstruction due to the collapse of the bronchioli and ducti alveolares, and how would this air disappear after a while unless it were absorbed by the circulatory blood? Therefore, we believe that there is no difference whatever in the production of atelectasis in the obstructed and in the compressed lung.

II. *Changes Produced in Entrapped Alveolar Air as Indicated by Successive Gas Analyses.*—The results obtained in closed as well as in open chest experiments show that within from two to seven minutes after bronchial obstruction the oxygen and carbon dioxide percentages fall rapidly to from 5 to 6 per cent; as seen in the tables, they remain at about the same figures until the complete disappearance of the alveolar air. Our results absolutely corroborate the results obtained under

TABLE 3.—*Changes in Oxygen and Carbon Dioxide Percentages After Obstruction*

Dog	Time After Obstruction	Oxygen	Carbon Dioxide	Comment
466	Before bronchial abstruction...	14.20	4.80	
	5 minutes.....	.....	4.09	
	35 minutes.....	2.09	4.12	Animal dyspneic and cyanotic
	2 hours, 50 minutes.....	4.00	5.30	
	2 hours, 20 minutes.....	5.70	6.07	Animal breathes quietly
475	10 minutes.....	3.90	6.40	
	25 minutes.....	3.90	4.70	
	50 minutes.....	16.70	3.09	Obstructing balloon broke
482	10 minutes.....	6.1	6.2	
	25 minutes.....	6.04	6.26	
	40 minutes.....	6.57	6.49	
	55 minutes.....	5.41	6.71	
	5 hours, 15 minutes.....	6.81	6.45	
	6 hours, 15 minutes.....	5.35	6.97	
	10 hours, 15 minutes.....	5.81	5.53	

similar conditions by Wolffberg and Loewy and von Schroetter. In table 3 are given the results we obtained on dogs.

The figures in table 3 show clearly that the oxygen and the carbon dioxide of the alveolar air tend rapidly to reach an equilibrium with the gases of the venous blood. Our figures correspond closely to those given by Wolffberg. It must be remembered that the latter represent the dry gases at 0 C.

The figures of Loewy and von Schroetter, obtained in the case of a patient, aged 31, with a catheter introduced through a tracheal fistula (case 31), are even closer to ours: before bronchial obstruction, oxygen 16.94 per cent, carbon dioxide 3.04 per cent; nine minutes after obstruction, oxygen 6.31 per cent, carbon dioxide 4.47 per cent; twelve minutes after obstruction, oxygen 5.55 per cent, carbon dioxide 4.86 per cent.

Furthermore, in animals in which gas analyses were performed until complete atelectasis occurred, the curves plotted for percentages of oxygen and carbon dioxide show that the percentages vary inversely so

that the curves cross one another (fig. 16). The same fact is shown by the figures given by Wolffberg and Loewy and von Schroetter, although it had not attracted the attention of these authors. Later we shall point out the importance of this point for our theory. From the foregoing considerations it is clearly seen that the entrapped alveolar air rapidly (in from one to fifteen minutes) undergoes marked qualitative changes, the percentages of oxygen dropping and of carbon dioxide rising, so that their respective partial pressures tend to come into equilibrium with the corresponding gases of the venous blood. These changes occur in exactly the same way in animals as in man.

III. *Is Entrapped Air Absorbed, and at What Rate?*—The qualitative changes of the entrapped alveolar air entitle us to deduce that quantitative changes in the mass of the gas must simultaneously occur and lead to its total absorption by the venous blood.

TABLE 4.—*Figures of Wolffberg*

	Oxygen	Carbon Dioxide
Experiment 2 (Wolffberg)		
Before bronchial obstruction	16.6	2.8
1 minute after obstruction	4.3	1.7
2 minutes after obstruction	3.1	1.9
3 minutes after obstruction	4.1	2.4
4 minutes after obstruction	3.3	3.2
5 minutes after obstruction	3.8	3.0
6 minutes after obstruction	1.6	5.1*
Experiment 1 (Wolffberg)		
Before bronchial obstruction	16.6	2.8
2 minutes after obstruction	3.2	3.1
3 minutes after obstruction	4.2	3.9
4 minutes after obstruction	5.0	3.3
6½ minutes after obstruction	2.7	4.2

* Dog has dyspnea.

In previous communications we have given abundant experimental evidence showing the production of typical atelectasis after complete bronchial obstruction. Roentgenographic, pathologic and histologic evidence has been given by many other investigators as well. A new contribution to this demonstration has been made by our experiments on animals with chests wide open and kept alive in our oscillating negative pressure box. The animal was in this box under conditions ideal for observation. The slightest changes in the physical characters of its lungs, aspect, color and size, could be recorded under direct vision before and after bronchial obstruction. Moreover, although the chest was wide open, the animal was under comparatively normal condition of respiration because its lungs were submitted to pressure variations exactly equal to pressure variations occurring in its intrapleural cavities before opening of the chest, and the respiration rate in the box was equal to its normal rate.

In our open chest experiments, atelectasis usually occurred within from six to ten hours, when the animal was able to withstand an experiment of such duration. The succession of events observed in these experiments is as follows: Immediately after successful obstruction

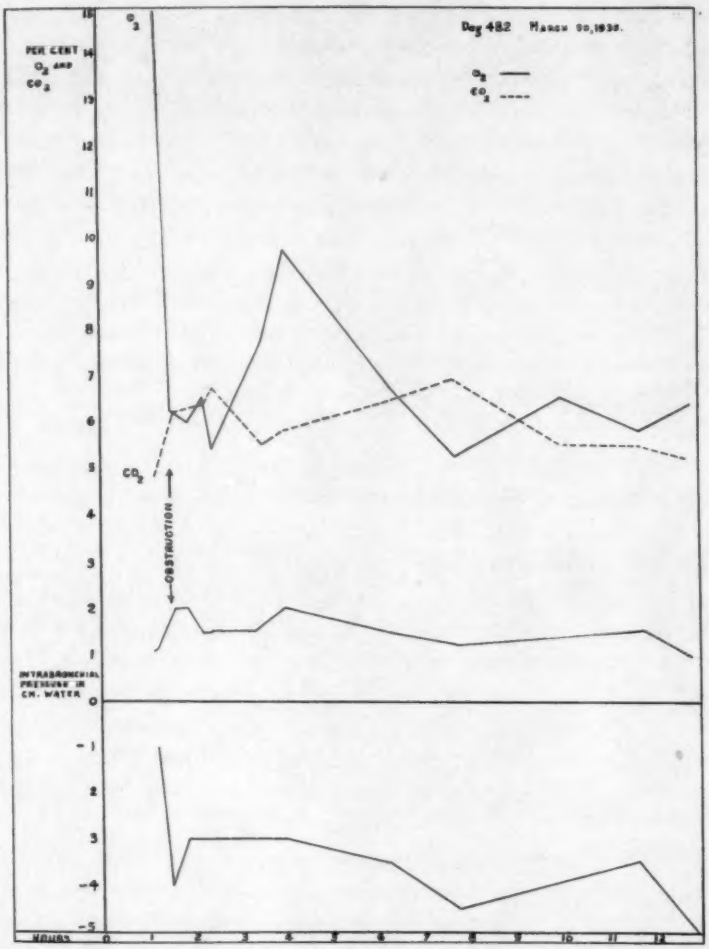

Fig. 16.—Graphic representation of percentages of oxygen and carbon dioxide obtained by alveolar gas analysis before obstruction and for a period of over twelve hours after obstruction of the right lung. The two lower curves represent the intrabronchial pressure variations in centimeters of water (one-half the actual pressure values; these figures represent the reading of one arm of the manometer).

"the lung stops breathing," whereas the normal lung increases in size. There is a slight inspiratory expansion in the occluded lung owing to the decrease of pressure (increased negative pressure) in the box during inspiration, but it is insignificant as compared to the wide res-

piratory movements of the other lung. Little by little the size of the occluded lung decreases as a whole, without a conspicuous change in its general shape, appearance or color. Gradually it sinks toward the costovertebral sinus, whereas the other lung increases in size so that the heart is manifestly displaced toward the obstructed lung. Except for a slight cyanotic hue, the obstructed lung does not show any other change until its volume is markedly decreased (to about one-fifth or one-seventh its original size). Then there appear dark bluish-brown patches scattered all over its surface without any special predilection for the hilus or the peripheral portion of the lung. We disagree in this respect with Van Allen and Adams, who claim that atelectasis proceeds from the hilus toward the periphery. We suspect that this happened in their dogs because they permitted a considerable amount of air to be extracted from the obstructed lung. After the great mass of gas is absorbed, atelectasis advances rapidly, and within approximately an hour is complete. Often small islands of slightly aerated light-colored parenchyma remain on the dark bluish-black atelectatic lung, the complete disappearance of which may take half an hour or more.[3]

That this atelectasis is due to absorption of the alveolar air by the circulating blood is proved by the following data:

(*a*) If a part of the entrapped alveolar air is aspirated through the cannula, atelectasis will occur more rapidly, the time being inversely proportional to the amount of air extracted.

(*b*) If the branch of the pulmonary artery corresponding to the obstructed lung is ligated, atelectasis will not occur. As a matter of fact, after this ligature the lung shrinks a little, and after several days becomes quite airless for weeks, because of fibrotic contraction; but as Schlaepfer and we have shown, the mechanism in this case is altogether different. The fact to keep in mind is, as Lichtheim long ago proved, that obstruction of a bronchus does not lead to atelectasis unless the circulation is intact.

(*c*) If after atelectasis has occurred we again introduce air into the atelectatic lung, not only does it regain its previous appearance, but also the same cycle of phenomena begins again, namely, qualitative and quantitative changes in the entrapped air and the production of atelectasis in exactly the same length of time if other conditions (general condition of the animal, circulation, respiration, etc.) remain the same.

(*d*) If instead of air other gases are introduced into the already atelectatic lung, the absorption time is different for each gas, depending on their respective coefficients of solubility and diffusion and the chemical affinity for the blood; this will be shown later.

3. The successive phases of atelectasis have been recorded in a cinematographic film.

(*e*) If an acute pathologic alteration of the lung endothelium is produced so that the respiratory membrane loses its permeability or the capillaries are damaged, atelectasis does not occur. This is shown in a remarkable way when ether in 100 per cent concentration is introduced into the atelectatic lung. Generally undiluted ether vapor is rapidly absorbed (100 cc. in one minute), but it produces a hemorrhagic edema (fig. 15) strictly limited to the obstructed portion of the lung. Further introduction of gas in this lung, even of carbon dioxide, which is usually rapidly absorbed, will not be followed by atelectasis. The lung has lost its functional ability for the exchange of gases through the alveolar and capillary endothelium. Production of atelectasis has become impossible. This fact is illustrated in experimental dog 499 (open chest), the protocol of which is given here.

Dog 499.—This animal weighed 15 Kg. Fifty-five milligrams of iso-amyl-ethyl barbituric acid per kilogram of body weight was given intraperitoneally.

April 30, 1930, 1:00 p. m.: The dog was in the oscillating negative pressure box (oscillations from —4 to —8).[4] The oscillation rate was 14 per minute. The heart rate was 116. One-quarter grain (16 mg.) of ephedrine sulphate was given hypodermically. The left lung was obstructed and washed out with oxygen.

4:15 p. m.: There was complete atelectasis of the entire left lung.

4:21 p. m.: Carbon dioxide was introduced to distend the left lung completely.

4:24 p. m.: The carbon dioxide was completely absorbed, and there was total atelectasis.

4:41 p. m.: One hundred per cent ether vapor was introduced to distend the lung to the size previously obtained with carbon dioxide (ether vapor was obtained by slowly passing liquid ether through a long metallic coil immersed in water at 90 C.).

4:45 p. m.: The left lung was edematous, of a dark pink to red color, and increased in size. Absorption was very slow.

4:47 p. m.: Oxygen was introduced into the left lung to distend it to its former size.

5:02 p. m.: There was no apparent absorption; the volume of the lung was the same.

5:06 p. m.: The clamp on the lung catheter was removed. A strong odor of ether came out of the catheter in a forceful stream of gas; the whole amount of oxygen introduced could be withdrawn, showing that no absorption of oxygen and probably of none of the ether had occurred.

Post Mortem: The left lung was pinkish red; in section it was very hemorrhagic and edematous. The weight of the right lung was 140 Gm.; of the left (edematous) lung, 232 Gm. Microscopic section showed interstitial hemorrhage (fig. 15).

The foregoing data offer indisputable evidence that the alveolar air below a bronchial obstruction is absorbed by the blood circulating

4. These figures are one-half the actual pressures and represent the readings of only one-half the manometer column.

through the alveolar capillaries, and that its disappearance occurs only in this way.

IV. *Speed of Absorption of Gases of Alveolar Air Introduced Individually into Atelectatic Lung of Living Animal and Gas Exchange That Takes Place Thereafter.*—A series of experiments was performed on dogs with both closed and open chest. In the first series (closed chest), after complete atelectasis of a lung or lobe had occurred following bronchial obstruction (as checked up by roentgenographic examination), oxygen was introduced. After complete atelectasis had occurred again, carbon dioxide was introduced.

This technic is extremely long because atelectasis requires from six to fifteen hours to be completed in the anesthetized animal; besides, many animals cannot withstand such a prolonged experiment under deep anesthesia. A much shorter method was therefore devised during our experimentation with the open chest. This consists in aspirating,

TABLE 5.—*Absorption Times of Oxygen and Carbon Dioxide Individually Introduced in a Lung Previously Rendered Atelectatic*

	Oxygen		Carbon Dioxide		
Dog	Cc.	Absorption Time, Min.	Cc.	Absorption Time, Min.	Comment
511	150	15	290	5	Closed chest experiment; roentgenographic control; other gases besides oxygen and carbon dioxide were successively introduced
	275	15	275	5	
	280	12	250	7	
507	...	..	100	2½	Open chest experiment
504	...	..	100	2	Open chest experiment
498	100	11	100	1	Open chest experiment
499	275	13	300	3	Open chest experiment

after obstruction of the bronchus of one lobe, as much alveolar air as possible and washing out the obstructed lobe by filling it with oxygen and emptying it from seven to ten times. In less than thirty minutes the lobe is completely atelectatic. The results obtained by following up the atelectatic lobe filled with oxygen and carbon dioxide are given in table 5. These experiments show that when these gases are introduced separately under atmospheric pressure their respective absorption times vary. What is more, these times are not always the same, varying according to the circulation rate and the permeability of the alveolar endothelium.

The figures in table 5 show that the absorption times of oxygen and carbon dioxide show a constancy which is in agreement with the physical laws of diffusion and solubility. These times, however, vary according to the anatomic conditions of the alveolar endothelium. This fact is well shown in dog 504, in the atelectatic lungs of which were successively introduced in the following order: nitrous oxide, carbon dioxide, ethyl chloride, ethylene, carbon dioxide, ethyl chloride, carbon dioxide,

ethylene, oxygen and ether vapor. Because of the lesions of pulmonary endothelium by the gases introduced in it, carbon dioxide at the first introduction was absorbed in two minutes; at the second introduction, in twenty-one minutes, and at the third introduction, in one hour and twenty-two minutes.

Nitrogen when introduced alone under atmospheric pressure into the atelectatic lung was absorbed within sixteen hours in dog 517. It is interesting to point out that whereas such a long time was required for its complete absorption, when introduced as the normal constituent of air (i. e., 80 per cent of atmospheric air) it is absorbed on the average in from six to fifteen hours. When pure nitrogen or other neutral gases are introduced into an atelectatic lung, gas analysis of the alveolar content shortly thereafter shows that oxygen and carbon dioxide are present in the same percentage as in the alveolar blood, that is, about 5 or 6 per cent each. From these facts it can be deduced, theoretically at least, that when after the introduction of pure nitrogen the oxygen and carbon dioxide have reached these figures, the absorption of the alveolar gases from this point on should proceed at the same rate as if air were now present.

V. *Results Following Introduction of Neutral Gases Separately Into the Atelectatic Lung.*—Nitrogen, hydrogen and helium were the gases used in these experiments.

Dog 517 (closed chest experiment).—This animal weighed 11 Kg. Iso-amyl-ethyl barbituric acid anesthesia was used and the left lower lobe bronchus obstructed.

5:30 p. m.: The left lower lobe was atelectatic.

5:45 p. m.: One hundred cubic centimeters of nitrogen was introduced.

9:35 p. m.: A specimen of gas contained 5.51 per cent oxygen and 7.34 per cent carbon dioxide. The nitrogen was completely absorbed in sixteen hours.

Dog 515 (closed chest experiment).—This dog weighed 12.5 Kg. Iso-amyl-ethyl barbituric acid anesthesia was used. The left bronchus was obstructed.

12:10 p. m.: The left lung was atelectatic.

12:40 p. m.: One hundred and five cubic centimeters of hydrogen was introduced.

4:30 p. m.: A specimen of alveolar air contained 6.16 per cent oxygen and 5.03 per cent carbon dioxide.

9:57 p. m.: A specimen of alveolar air contained 5.50 per cent oxygen and 6.38 per cent carbon dioxide. The hydrogen was almost completely absorbed in eighteen hours.

Dog 510 (closed chest experiment).—This dog weighed 22 Kg. Iso-amyl-ethyl barbituric acid anesthesia was given. The left stem bronchus was obstructed.

8:30 a. m.: Atelectasis was complete. One hundred and seventy-five cubic centimeters of pure helium was introduced into the left lung.

9:30 a. m,: Gas analysis showed 5.83 per cent oxygen and 9.34 per cent carbon dioxide.

1:00 p. m.: Gas analysis showed 5.34 per cent oxygen and 6.22 per cent carbon dioxide.

2:10 p. m.: Gas analysis showed 5.25 per cent oxygen and 6.64 per cent carbon dioxide. The helium was completely absorbed in twenty-six hours.

Dog 507 (open chest experiment).—The animal weighed 12 Kg. Iso-amyl-ethyl barbituric acid anesthesia was used. The left bronchus was obstructed.

2:00 p. m.: Atelectasis of the left lung was complete. One hundred and fifty cubic centimeters of helium was introduced into the left lower lobe.

2:20 p. m.: Gas analysis showed 2.66 per cent oxygen and 4.54 per cent carbon dioxide.

5:45 p. m.: Gas analysis showed 2.83 per cent oxygen and 5.03 per cent carbon dioxide.

7:52 p. m.: The dog died. Little helium was absorbed.

TABLE 6.—*Exchange of Alveolar Gases as Shown by Carbon Dioxide and Oxygen Determinations After Introduction of Various Cases Into an Obstructed Lobe of the Lung*

Gas	Dog	Description	Time	Carbon Dioxide, per Cent	Oxygen, per Cent
Helium	507	Vacuum box experiment: left lower lobe washed out nine times with oxygen and allowed to become atelectatic; 150 cc. of helium was introduced into it at	2:00 p.m.		
			2:10 p.m.	4.54	2.66*
			5:45 p.m.	5.03	2.83*
Helium Oxygen	510	Closed chest experiment: the left lower lobe was obstructed and allowed to become completely atelectatic; 200 cc. of a mixture of equal volumes of helium and oxygen was then introduced into it at	5:50 p.m.		
			8:00 p.m.	5.86	8.29
Helium		This lobe was now washed out three times with pure helium and 175 cc. of helium was introduced into it at	8:30 p.m.		
			9:30 p.m.	9.34	5.83
		The next day at	1:00 a.m.	6.22	5.34
			2:00 a.m.	6.64	5.25
Hydrogen	515	Closed chest experiment: the left lower lobe was washed out seven times with oxygen and allowed to become atelectatic; then 105 cc. of hydrogen was introduced into it at	12:41 p.m.		
			4:30 p.m.	5.03	6.16
			9:57 p.m.	6.38	5.50
Nitrogen	517	Closed chest experiment: the left lower lobe was obstructed and washed out three times with nitrogen by aspiration and distending it with pure nitrogen after each aspiration; then 100 cc. of nitrogen was introducted into it at	5:45 p.m.		
			9:35 p.m.	7.34	5.51

* These are unusually low figures for alveolar oxygen probably due to poor respiration and anoxemia.

We have also introduced various gases into the pleural cavities of dogs and rabbits. In the dog we have not been able to produce a unilateral pneumothorax with air, owing to the permeability of its mediastinum. However, with helium we have been able to produce a temporary unilateral pneumothorax. In the rabbit in which the mediastinum is more like that of man, we have, of course, been able to produce unilateral pneumothorax with air, nitrogen and helium.

Table 6 is a résumé of these experiments.

The foregoing experiments show that a short while after the introduction of neutral gases into the atelectatic lung, oxygen and carbon

dioxide diffuse through the alveolar membrane from the venous blood so that these gases are present in the alveoli under the same partial pressures as in the blood.

When a mixture of equal parts of a neutral gas and oxygen or carbon dioxide is introduced into the atelectatic lung, the same phenomenon of rapid establishment of gas equilibrium occurs.

Dog 510.—5:50 p. m.: Two hundred cubic centimeters of equal parts of helium and oxygen by volume was introduced into the atelectatic left lung.

7:20 p. m.: Gas analysis showed 5.86 per cent oxygen and 8.29 per cent carbon dioxide.

The same modifications in the percentages of alveolar gaseous content occur when more active gases (oxygen, carbon dioxide) are introduced individually into the atelectatic lung.

Dog 498 (open chest experiment).—This dog weighed 6.5 Kg. Iso-amyl-ethyl barbituric acid anesthesia was used. The left bronchus was obstructed.

10:40 p. m.: One hundred cubic centimeters of oxygen was introduced into the atelectatic lower left lobe.

10:50 p. m.: Gas analysis showed 8.59 per cent oxygen and 8 per cent carbon dioxide.

VI. *Behavior of Respiratory Membrane Toward Anesthetic Gases or Vapors* (Nitrous Oxide, Ethylene, Ethyl-Chloride, Ether Vapor).—The protocols show the approximate absorption times, by the alveolar endothelium of lungs previously rendered atelectatic, of the most usually used anesthetic vapors or gases. This question is still under investigation; with the vacuum box method, in using lungs previously rendered atelectatic, the absorption time can be checked by direct observation. These results will be published later.

VII. *Changes, if Any, in Intrapulmonary Pressure in Occluded Lung During Process of Gas Absorption.*—The prevailing idea concerning the intrapulmonary pressure on the affected side in obstructive atelectasis is that it should be more "negative" than normally, because of the shrinkage of the affected lung and the "sucking in" of the other lung, heart and diaphragm in the thus liberated space. It is generally believed that this negative pressure should increase with the progress of atelectasis, reaching its maximum figure at the completion of atelectasis. As a matter of fact, we have found no significant changes in the intrapulmonary pressure. Figure 17 gives the smoked drum tracings of both the intrapulmonary and intrapleural pressures in dog 422 for a period of over three hours. It is seen that these pressures are constant.

Loewy and von Schroetter came to similar conclusions after obstructing a bronchus in man. "The pressure," they said, "in the obstructed lung does not show a gradual fall. Not only does it remain constant

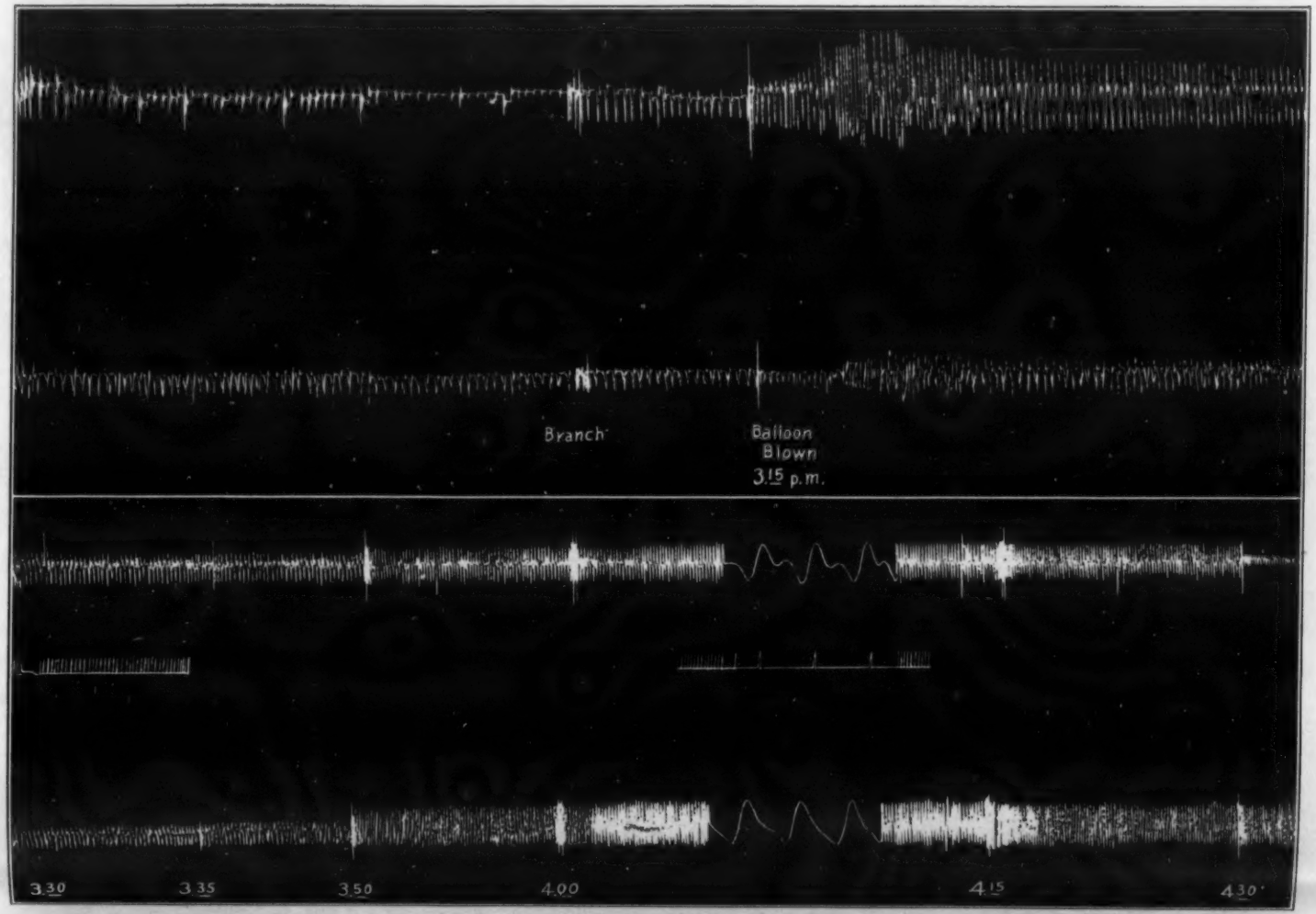

Figure 17 A and B

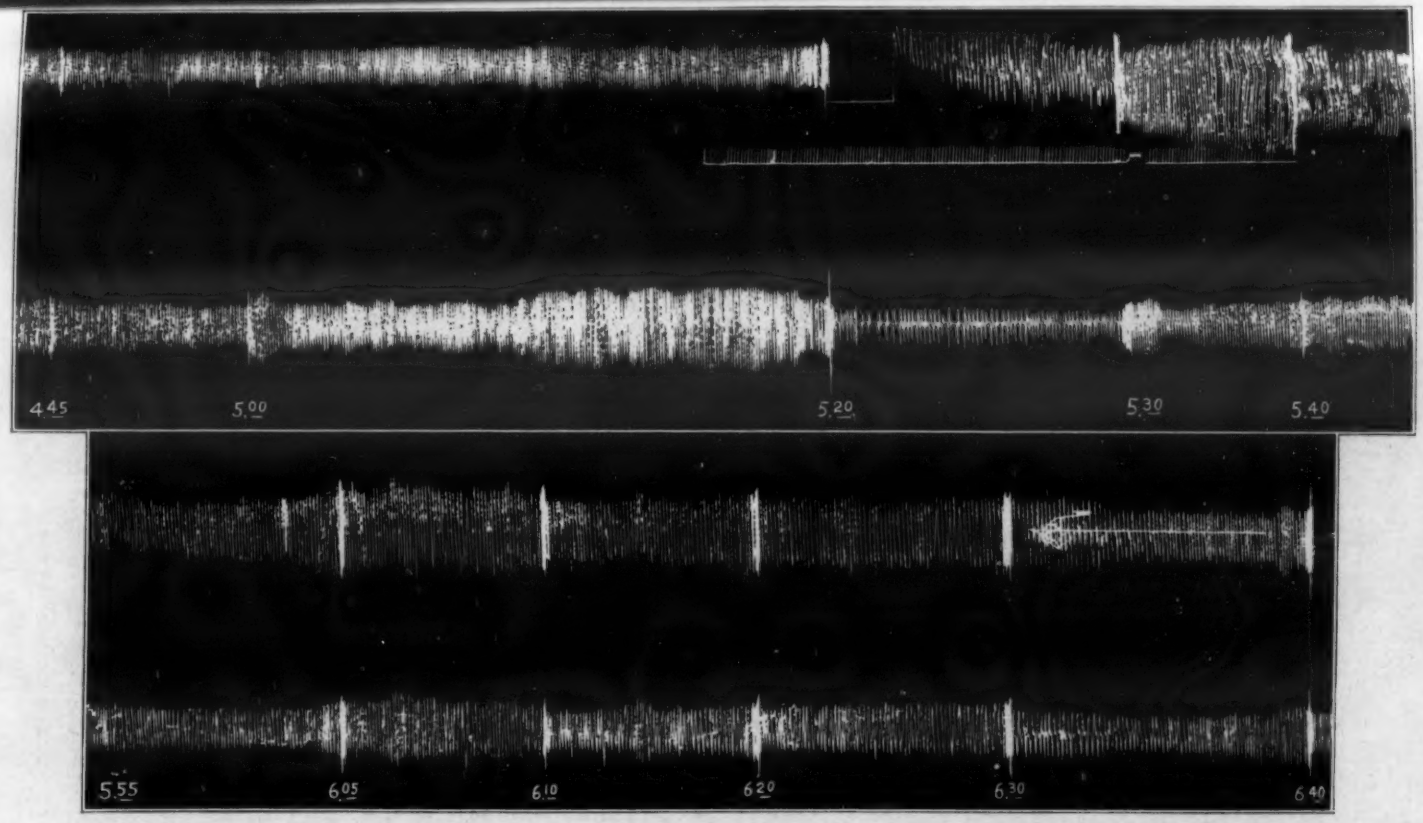

Figure 17 C and D

Fig. 17 (dog 422).—Obstruction of right lower lobe. Parts of a continuous tracing of intrapulmonary and intrabronchial pressures for a period of over three hours. An intrapleural cannula was introduced into the right pleura and connected to a mercury manometer recording on a smoked drum (lower curve). The larger tube (intrapulmonary) of the bronchial catheter was connected to another manometer recording on the same smoked drum (upper curve). No changes in pressure occurred for a period of over three hours after bronchial obstruction. The arrow indicates time in seconds.

but even when relatively large amounts of air, as referred to the total air, are rapidly withdrawn for gas analysis, the pressure instantly comes back to normal." They repeated this investigation on four human cases with similar results. These experimental data are only apparently in conflict with the recently reported greatly increased intrapleural negative pressure in cases of atelectasis. We shall discuss this important point under "Comment."

OUR THEORY OF PRODUCTION OF ATELECTASIS

The experimental study of the exchange of gases in the obstructed lung leads to the conclusion that the disappearance of alveolar air is due to its absorption by the circulating blood; axiomatically, the reverse seems also true, that apneumatosis cannot result unless the alveolar gases are shut off from the external air. In compression atelectasis (pneumothorax, pleural fluid, etc.), the collapsed alveolar bronchioli

TABLE 7.—*Percentages and Partial Pressures of Oxygen, Carbon Dioxide and Nitrogen in Alveolar Air and Venous Capillary Blood*

	Alveolar Air		Venous Blood	
Gas	Per Cent	Partial Pressure in Mm. Hg	Per Cent	Partial Pressure in Mm. Hg
Oxygen	15	114	5	38.0
Carbon dioxide	5	38	6	45.6
Nitrogen	80	608	..	608.0

become occluded and this occlusion should be complete if atelectasis is to occur. Mere narrowing of the bronchi or bronchioli, from whatever cause, cannot produce atelectasis; on the contrary, it causes emphysema. The foregoing data render possible the elaboration of a theory on the production of atelectasis which is simple, comprehensive and based on such sound physiologic and physical factors as the laws regulating the exchange of gas between alveolar and venous air.

Table 7 represents in round figures the percentages and the corresponding partial pressures of gases in the alveolar and venous air. These differences in partial pressures are possible notwithstanding the continous exchange of gases through the respiratory membrane, only because the alveolar air is continuously renewed by respiration, drawing by diffusion on the tidal air filling in each respiration the dead space and bronchi. This exchange is so active, that in spite of the continuous renewal of air, the alveolar air is poorer in oxygen and richer in carbon dioxide than the atmospheric air. It is precisely the differences in partial pressures between alveolar and venous gases which render possible oxygenation of the venous blood and elimination of its carbon dioxide.

It is obvious, then, that if a bronchus is obstructed the air entrapped in the lung will undergo qualitative changes. Its composition will gradually approach the percentages of the gases of the venous blood which is constantly coursing around the alveoli, carrying away gases which are under excess pressure in the alveoli (oxygen) and giving off gases to the alveoli which it has in excess (carbon dioxide). Such qualitative changes necessarily result in quantitative changes.

In order to simplify the question, we shall graphically represent the alveolus by a circle surrounded by a larger circle which represents the venous blood circulating in the perialveolar capillaries (fig. 18). Further, 100 will represent the volumes of a gaseous content of this alveolus. After obstruction of the bronchiolus, an equilibrium of gases inside and outside of the alveolus will be established. We shall consider the three gases separately.

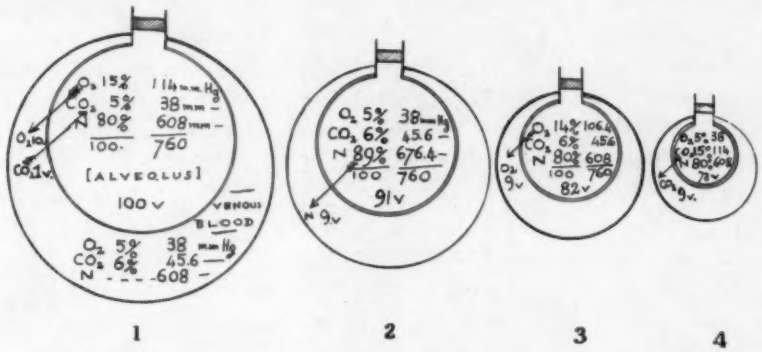

Fig. 18.—A schematic representation of alveolar gas exchanges, gradual gas absorption and shrinkage of the alveoli after complete bronchial obstruction. The absolute volume of the alveolus is only approximately indicated, but the figures given are relative and demonstrate perfectly well the principles involved. In *1*, ten volumes of oxygen diffuse into the venous blood and one volume of carbon dioxide diffuses out of the venous blood into the alveolus. In *2*, the alveolus has now lost nine volumes of gas as stated under (*1*) and the oxygen and carbon dioxide have come into equilibrium in the venous capillary blood and in the alveolus. However, the percentage and partial pressure of nitrogen have now been increased so that nine volumes of nitrogen diffuse out of the alveolus into the venous blood. In *3*, nine volumes of nitrogen having previously diffused out of the alveolus into the venous blood, the percentage and partial pressure of oxygen or carbon dioxide have been relatively increased. For purposes of explanation let us say the oxygen has been thus relatively increased in percentage and partial pressure. Nine volumes of oxygen are now ready to diffuse out of the alveoli into the venous blood. In *4*, nine volumes of oxygen having diffused from the alveolus into the blood, we can now consider that the carbon dioxide in the alveolus is relatively increased by these nine volumes. Thus the partial pressure of this gas is relatively increased and carbon dioxide is ready to diffuse out of the alveolus. Thus the cycle continues until all the gases of the lung are absorbed, although actually the gas exchanges are going on simultaneously and not in the isolated way which we have ideally considered.

Oxygen represents 15 per cent of the gas mixture and it is under a partial pressure of 114 mm. of mercury in the alveolus, whereas in the venous blood it is present to the extent of 5 per cent and a partial pressure of only 38 mm. of mercury (fig. 21). Therefore, 10 volumes of oxygen will pass from the alveolus into the blood; at the same time, and for similar reasons, 1 volume of carbon dioxide will pass in the opposite direction from the blood to the alveolus. In this way the gas mixture of the alveolus will lose 9 per cent of its original volume, so that instead of 100 volumes there is now 91 volumes. Now if the alveolar wall were a rigid structure, the total pressure of gas in the alveolus would decrease and instead of a pressure of 114 plus 38 plus 608 = 760 mm. of mercury, it would become 38 plus 45.6 plus 608 = 671.6 mm. of mercury. Since the alveolar wall is a perfectly elastic structure, it is obvious that under these circumstances the alveolus will retract down for two reasons: (1) because of the elasticity of the alveolar membrane and (2) because of the outside intrathoracic pressure. The other lung being in connection with the atmospheric air, the intrathoracic pressure on that side is 760 mm. of mercury (the negative intrapleural pressure of from —4 to —7 mm. of mercury is comparatively so small that it is of little importance in this mechanism (fig. 18).[2]

We shall now consider nitrogen. At the start, before bronchial occlusion, it represented $^{80}/_{100}$ of the alveolar gas mixture. Now after the reduction in volume of the gas mixture, it represents $^{80}/_{91}$ of the gas mixture and its partial pressure has risen to 676.4 mm. of mercury. But this pressure is much higher than the pressure of nitrogen in the capillary blood; the excess of nitrogen will therefore pass into the blood. In other words, 9 volumes of nitrogen will be carried from the alveolus by the circulating blood, so that the volume of the alveolar air will be 91 — 9 = 82 volumes [5] (fig. 18).[3]

This decrease in alveolar nitrogen disturbs the equilibrium of oxygen and carbon dioxide between the alveolar air and the venous blood. Now suppose that oxygen alone is affected by this imbalance. It is obvious that instead of 5 per cent, as it was previously, it will now represent 14 per cent of the alveolar gas mixture (N_2 80 + CO_2 6 + O_2 14 per cent), and therefore its partial pressure will rise to 106 mm. of mercury; so that now again 9 volumes of oxygen are ready to be carried away from the alveolus by the circulating blood. When this happens, the volume of the alveolus will decrease to 82 — 9 = 73 volumes.

5. These figures are not, strictly speaking, exact; for example, 80/91 = 87.9/100 and the partial pressure corresponding to it equals 667.04 mm. of mercury. We prefer to give the figures as they are, however, because they simplify the explanation without altering any essential relations between the gases.

The carbon dioxide will be affected in the same way (fig. 18),[4] and for similar reasons its percentage will rise from 6 to 15 per cent, corresponding to a partial pressure of 114 mm. of mercury, so that again 9 volumes of carbon dioxide are ready to be carried away by the circulating blood, thus reducing the volume from 71 to 62. The cycle is repeated, and 9 volumes of nitrogen will be ready to pass from the alveolus into the venous blood. Continuing this series of events, there will be a constant oscillation in gas values, and all the alveolar gases will be absorbed. In the open chest experiments we have noted that the initial absorption of gas is slow; after a while the lung seems to shrink much more rapidly; that is, there is an accelerated diminution in the size of the lung. Toward the end of the process when the great

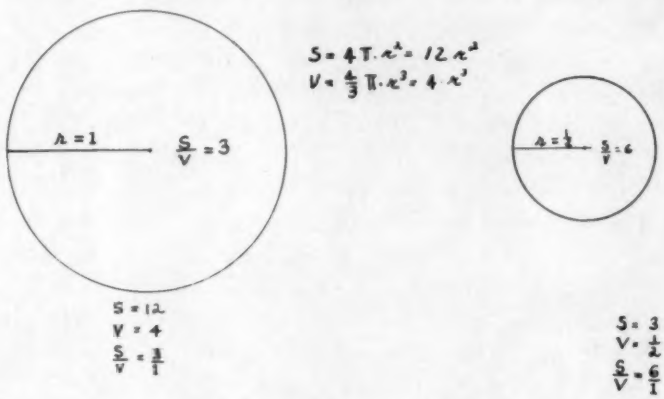

Fig. 19.—Showing the mathematic acceleration in absorption rate of gases in the alveoli of the lung. These relations probably hold true up to a point where the capillary circulation is definitely impaired.

mass of gas has already been absorbed, the process of absorption seems to slow down markedly, so that one may observe small isolated or patchy areas remaining practically unchanged over a long period of time. This mechanism is explained in figure 19. The alveolus is represented by a sphere the radius of which is 1. The ratio of surface to volume is 3:1. Now suppose gases are absorbed so that the alveolus shrinks and its radius is one-half; the ratio of surface to volume is now 6:1. In other words, the volume of contained gases has been diminished much more than the surface of the alveolus, and there is relatively twice as much surface for the contained volume of gas as there was previously. This means that there is more absorbing surface for a unit volume of gas, and the alveolus will absorb a greater fraction of its contained volume of gas per unit of time than in the previous

case. Thus with the progressive shrinkage of the lung there is an acceleration in the absorption rate. However, this effect is offset by the impoverishment of the capillary circulation when the alveoli are markedly collapsed, so that in this way we can explain what we have actually observed—a slowing up of absorption toward the end of the process.

It is understood, of course, that gas absorption does not occur in the schematic way we have here depicted; actually, there is an incessant simultaneous exchange of all the gases involved. Bohr has shown that extremely small differences in partial pressures are sufficient to insure the diffusion of great amounts of gases through semipermeable membranes. A difference of only 1 mm. of mercury suffices for the passage through the alveolar membrane of the 300 cc. of oxygen per hour per kilogram necessary basically for a man at rest.

We have seen that the anesthetic vapors and oxygen are rapidly absorbed. It is now easy to understand how atelectasis might develop during the course of an operation as in the cases reported by H. Santee and Bergamini and Shepard. Should complete bronchial obstruction by secretions occur during the course of an operation and the lung area involved contain a high percentage of anesthetic vapors and oxygen, atelectasis could readily be produced within a short time.

A word should be said further about the rôle played by nitrogen in the gaseous exchanges in the lung. We have seen that it is one of the inert gases, requiring many hours for its absorption. Oxygen and carbon dioxide alone are absorbed by the lung in a relatively few minutes; but when oxygen and carbon dioxide are considered in the atmospheric mixture their absorption periods are greatly prolonged, the nitrogen of the air acting as a physical brake by virtue of its slow absorption into the blood. For this reason should bronchial obstruction occur, the time required for the production of atelectasis would be measured in hours rather than minutes. In this way the nitrogen of the air may be considered as a fortunate circumstance of nature to delay alveolar gas absorption and production of atelectasis. This delay is valuable because it allows an interval of time during which reaeration of the lung could still be easily accomplished. Thus nitrogen may be thought of as the "safety brake," especially during anesthesia and the postoperative period, and may be considered as the "buffer" of the air.

From the foregoing paragraphs it is seen that in the absorption of anesthetic gases and vapors the nitrogen of the air allows their dilution and acts as a mechanical "buffer," delaying their absorption. We think it safe to state that but for the nitrogen of the air, inhalation anesthesia would be so full of danger as to be impracticable.

COMMENT

There are three possible objections to the theory:

1. An equilibrium between the gases of the blood and alveolar blood could be reached after bronchial occlusion, and this should stop further exchange of gases.

2. Much more carbon dioxide should pass from the blood into the alveoli, because its speed of passage through the alveolar membrane is thirty times as great as for oxygen; thus atelectasis would be impossible.

3. The negative intrapleural pressure has often been reported so great that it should cause a passage of gases from the blood into the alveolus and in this way prevent atelectasis.

The first objection can easily be answered. If all the gas molecules are absorbed, this is due to the perfect elasticity of the alveolar membrane and to the great difference in diffusion speeds through it of oxygen, carbon dioxide and nitrogen. For these reasons a perfect equilibrium is never reached, and as Loewy and von Schroetter first showed, the exchange of gases are represented by an asymptotic curve.

The second objection is based on the great speed of passage of carbon dioxide through the alveolar membrane as compared to oxygen or nitrogen. We have already mentioned the experiment of Loewy and Zuntz with the frog's lung demonstrating this point. Exner, using a soap film, showed that carbon dioxide would pass through it toward an indifferent gas with a speed of about 10 cc. per minute per square centimeter when under a pressure of only $\frac{1}{2000}$ of an atmosphere. But the rate of diffusion of gases is regulated by their partial pressures, so that, although carbon dioxide passes rapidly from the blood into the alveolus after bronchial obstruction, an equilibrium is reached when its percentage becomes about 6 per cent in the alveolus; after this point the actual mass of carbon dioxide exchanged through the respiratory membrane is stopped. In other words, the exchanges of carbon dioxide are rapidly accomplished, but the actual amount of carbon dioxide passing through the respiratory membrane is regulated exclusively by the differences in partial pressure of the gases respectively, in the alveolar and venous air.

The third objection is of even greater importance. Habliston, in 1928, found the intrapleural pressure on the atelectatic side in four cases in man to be -12, -13, -16 and -25 mm. of mercury respectively, as against -4 to -7 mm. on the unaffected side. Farris reported two similar cases in which relief was obtained by artificial pneumothorax. Wilson and Gordon (quoted by Habliston) and Ashbury have also reported such cases. Ashbury reported a case with a negative intrapleural pressure of -16 to -20 mm. of mercury; after

inducing a partial pneumothorax on the affected side with 600 cc. of air, the pressure became —4 to —7 mm. of mercury.

Presumably, with a negative intrapleural pressure of —16 to —20 mm. of mercury the intrapulmonary pressure is also —16 to —20 mm. of mercury below atmospheric pressure, for the gases in the lung are under a pressure which tends to be equal to the intrapleural pressure.

It is interesting to compare these figures to our own data on dogs and the data of Loewy and von Schroetter on man, in which the pressure of the entrapped alveolar air did not change. From the cases of the latter authors, it can be deduced that the intrapleural pressure on the affected side also remains constant. The explanation for these discrepancies in the intrapleural pressures between the dog and man is that in the dog both intrapleural pressures are equal because of the elasticity and permeability of the mediastium. It might be objected that the longest period of bronchial obstruction carried out by Loewy and von Schroetter was only forty-two minutes—a time insufficient for the production of atelectasis.

In the case of a lung which is completely obstructed the pressure of gases within it tends to equal the intrapleural pressure because of the elasticity of the alveoli; thus, if the intrapleural pressure were —20 mm. of mercury, the intrapulmonary pressure would also be about 20 mm. of mercury less than atmospheric, i. e., about 740 mm. of mercury. If we consider the percentages of oxygen and carbon dioxide in the entrapped alveolar air as 5 and 6 per cent, respectively, their partial pressures would be 38 and 45.6 mm. of mercury when the intrapulmonary pressure is 760 mm. of mercury, and 37 and 44.4 mm. of mercury with an intrapulmonary pressure of 740 mm. Therefore, in the case under consideration, the effect of a —20 mm. negative intrapleural pressure would be to lower the partial pressure of oxygen and carbon dioxide in the alveolus by only from 1 to 2 mm. However, it must also be remembered that the gases in the alveolar capillary blood are also subjected to corresponding diminution in their pressures, so that from a relative standpoint the partial pressures of the gases in the alveoli and in the alveolar capillaries have not changed. We may thus deduce that the increased negative intrapleural pressure does not materially influence the exchange of gases in the obstructed lung.

So far as the therapeutic effect of artificial pneumothorax is concerned, we agree with the foregoing authors quoted as to its palliative effect by decreasing the displacement of the heart but we completely disagree as to its efficacy in freeing the air passages from obstructing material. Pneumothorax cannot further compress a lung already atelectatic. Lastly, collapse of the lung by pneumothorax does not favor reaeration or penetration of air into this lung; on the contrary, deeper

respiration by producing dilation of the bronchi is more apt to lead to the formation of airways between obstructing mucus and bronchial wall with subsequent expulsion of the obstacle to respiration.

Increased pressure of the entrapped air as produced in coughing or strained respiration would theoretically accelerate the absorption of the alveolar gases, as has been maintained by Van Allen and Adams. We think, however, that these authors have greatly exaggerated the importance of the factor, for an increase in intrapulmonary pressure in the obstructed lung can in these cases be produced only by an increase in the intrapulmonary pressure of the healthy lung. This means an increase in total intrathoracic pressure and consequently in the blood and blood gases as well. It seems that in these cases of Van Allen and Adams, if atelectasis was produced earlier in animals incompletely anesthetized and struggling, this was due rather to excessive muscular work and exhaustion of oxygen in the blood, while at the same time rapid breathing washed out the carbon dioxide of the blood; the percentages of both gases and their partial pressures in the blood were decreased, causing a more rapid absorption of the entrapped air. We do not think, however, that from their data these authors were justified in coming to the conclusion that "narcotics are advisable because they aid in preventing atelectasis." The chief means the lung possesses to prevent atelectasis, or to overcome it once the bronchus is obstructed, is expulsion of the bronchial exudate by cough and deep breathing. Narcotics, on the contrary, deprive the lung of its best means of defense. We believe that for reasons previously described, the more efficient treatment (both preventive and curative), besides rolling of the patient from side to side and encouraging him to breathe deeply, is hyperventilation by repeated inhalation of 10 per cent carbon dioxide in oxygen, according to the method introduced by Henderson and Haggard in resuscitation after carbon monoxide poisoning, or bronchoscopic aspiration of bronchial exudate.

For a number of years, we have endeavored to show that atelectasis is a well defined clinical syndrome with a definite etiology, pathogenesis, pathology and treatment. It presents various clinical forms which can briefly be distinguished as follows:

1. According to the etiology: obstructive or compressive, postoperative or medical.
2. According to its distribution: multilobar (massive), lobar or lobular (patchy).
3. According to its duration: acute or chronic.
4. According to its evolution: simple or complicated.

The last variety comprises the cases in which infection follows because of the presence of the obstructing agent of microbes of more or

less high virulence, so that an infectious process begins in the lung and is favored by the impaired drainage of the respiratory organ. Postoperative atelectasis in which group 4 pneumococcus is always present represents a mild form of infection. Lobar pneumonia, in which more virulent pneumococci are present, represents another type of acute infectious atelectasis occurring as an accident in the course of a pneumococcic bronchitis. Abscess and gangrene of the lung are similarly infectious forms of septic bronchial obstruction and atelectasis, due to specific micro-organisms: aerobes and anaerobes. The painstaking work of Smith, Allen, Joannides and others throws a new light on this last variety, justifying our conception.

We have also endeavored to prove that the pathologic process in the different forms of atelectasis develops along the same lines as in similar lesions in glandular organs the ducts of which have been obstructed and to which the lung should be compared. We have shown that the circulation and the ventilation in lungs that have become atelectatic from any cause show exactly parallel changes, depending entirely on the condition of the pulmonary ventilation.

The present work, by showing the intimate mechanism of the production of apneumatosis, can explain the pathogenesis of the different forms of the disease by sound physiologic principles. It shows, further, the importance of physiologic, physical and chemical consideration in the study of respiration in relation to thoracic surgery. Clinical and experimental evidence points to the conclusion that atelectasis is always due to complete bronchial obstruction. We wish to stress the great importance in the pathology of the lung of impairment of free bronchial drainage, and we believe that it has been demonstrated beyond doubt that atelectasis must be definitely associated with the idea of bronchial obstruction. The obstructing agent, whatever its nature, should be sought and treatment instituted for its removal and reaeration of the lung.

CONCLUSIONS

1. An experimental method has been devised which gives evidence that when a bronchus is completely obstructed, the entrapped alveolar air rapidly undergoes qualitative and quantitative changes as determined by successive gas analyses.

2. Qualitatively, the percentages and partial pressures of the gases comprising the alveolar air tend to, but never quite, reach an equilibrium with the gases of the venous blood.

3. Quantitatively, the entrapped alveolar gases pass through the respiratory membrane into the blood circulating in the perialveolar capillaries until complete airlessness of the involved area is produced.

4. The mechanism of production of atelectasis in the compressed lung (pneumothorax, pleural exudate, intrathoracic tumors, etc.) is exactly the same as in bronchial obstruction.

5. Besides the gases of the air, diffusion of other gases were studied by introducing them into a lung previously rendered atelectatic. The different gases used in these experiments were: (*a*) active gases, oxygen and carbon dioxide; (*b*) neutral gases, hydrogen, nitrogen and helium; (*c*) anesthetic gases or vapors, ether, ethyl chloride, nitrous oxide and ethylene.

6. A new experimental method was devised which allows direct vision of the pulmonary changes occurring during the experiment.

7. Nitrogen in the respiratory air plays the part of a mechanical "buffer," retarding the absorption of more diffusible and more soluble gases.

8. This experimental work has allowed the formation of a theory on the mechanism of atelectasis based on the physiology of exchange of gases in the lung.

Mr. Eugene Ostrow and Dr. Wade Duley gave us technical assistance; Miss Helen C. Warny of the Airo-Balloon Corporation, New York City, supplied the helium gas; Mr. W. S. F. Dunn and Miss Rosamond McPherson assisted with photographs; Mrs. Aies Larsen prepared the histologic sections.

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ABSTRACT OF DISCUSSION

DR. W. E. LEE, Philadelphia: When we recently called attention to the unusual incidence of asthma and allergy in patients in whom postoperative atelectasis developed, and suggested that here might be a predisposing factor that would have to be considered, one of our critics accused us of unnecessarily complicating the simple explanation that bronchial obstruction was the only cause of this phenomenon.

After hearing this paper by Dr. Van Allen and his co-workers, I am sure that every one will feel that he is open to the same criticism. He certainly raises doubt as to obstruction being the only cause of atelectasis. I think that he presents evidence that this is not a simple problem but a difficult and complicated one.

For some time we have been convinced that obstruction is not the only factor concerned, and that it is not the primary etiologic factor but a late determining cause of atelectasis.

Dr. Van Allen's explanation of the confusing experiences that we have all had with this work—the inconstant results that follow efforts to maintain an airway in the bronchi by coughing and the irregularity with which atelectasis follows bronchial obstruction—requires careful consideration. The dependence of the cough reflex and the result of expiratory effort on the presence of what he calls "available air" distal to the obstruction is a new thought. In order that an obstruction may be driven away from the periphery by coughing, it is necessary that "available air" be distal to the obstruction to drive it toward the larger bronchi. This would fit in perfectly with our claim that it is necessary to maintain or to obtain an airway in the bronchi to prevent or relieve atelectasis. This is what we have accomplished in our bronchoscopic drainage in cases of obstruction. It is what Santi probaby accomplishes when he changes the position of the patients, dislodges the obstructing mass and establishes an airway. It is what Gibson in New York probably accomplishes when he thumps and beats his patients, and what Scott, Henderson and Coryllos accomplish when they increase the depth of the respiratory movements by inhalations of carbon dioxide.

There is one phase of this work of Van Allen's which has worried me a great deal and that is the question of cough. In a previous paper he claimed that in order to produce obstructive atelectasis one must have resisted cough. I feel that one should separate cough into two types. I fully agree with him that in "unproductive cough," when the obstruction is not relieved, the inspiratory effort which follows the unproductive effort forces, and the negative pressure in the obstructive tissues draws, the obstruction toward the periphery.

On the other hand, "in productive cough" there is sufficient air or "available air," as Van Allen calls it, behind or peripheral to the obstruction, to clear the bronchial tubes of the secretions and to maintain an airway and thus allow reaeration of the lung.

Thus Van Allen's demonstration of the presence of "available air" in the pulmonary tissues distal to an obstructed bronchus which comes from the adjacent

alveoli of an unobstructed lobe fits into our clinical observations. In other words, is this not a physiologic provision on the part of nature to provide the adequate "available air" behind or peripheral to obstructing bronchial secretions that makes the productive cough efficient? What would happen to the human race if one did not have a productive cough? I feel that although on first sight this looks entirely at odds with clinical experience, it fits into it very well if one divides cough into two types, as clinicians have done for many years, giving sedatives for the unproductive cough and stimulants for the productive cough.

Dr. Howard Lilienthal, New York: I am absolutely unable to criticize or in a scientific way to comment on the excellent demonstrations that you have seen here. I must confess that I was a bit shaken up by Dr. Van Allen's exposure of the apparent impossibility of producing lobular atelectasis by plugging the bronchus. I do know something, however, about what the lung looks like when the chest is opened. I have operated on the chest in suppurative disease; I have operated on it for tumor and for various other conditions exclusive of the empyemas.

I have noticed repeatedly, and I am sure that all of you who have performed operations of this kind must have noticed, that there are occasionally, especially in the lower lobes, spots of atelectasis plainly marked out by pittings several centimeters in diameter, and that these spots of atelectasis are by no means confined to large areas of the lung, but may occur in perhaps fifteen or twenty different places on the surface of the lung and resemble cicatrices. By increasing the intrapharyngeal pressure the lung can gradually be distended, and these atelectatic spots can be blown up to the normal size and color of the lung.

I am not going to try, after what I have heard today, to make any explanations. I shall only say again what I suggested in 1919, after my work at the front during the World War when I performed operations on a good many chests, that this sort of atelectasis, which we at that time called traumatic atelectasis, is probably due to a spasm of the lung, and I see no reason why I should give up that opinion. I believe that a condition inherent in the lung—an idea that some one else hinted at today—produces this form of atelectasis, and not necessarily obstruction of some kind. If there were an obstruction, active inflation of the lung would simply accentuate the atelectasis by filling the other parts of the lung and leaving the atelectatic patches, because they are obstructed. But they, too, can be blown up, and the lung attains its normal appearance and size.

I offer these remarks simply that Dr. Van Allen and the others who are working on this extraordinarily interesting subject may, if they wish, take this view into consideration.

Dr. C. M. Van Allen, New Haven, Conn.: I should like to leave one idea with you, namely, that atelectasis is complicated. It is not a simple affair of blocking and absorption of air. I heartily agree with Dr. Lilienthal in his remarks and Dr. Lee in regard to the other factors that may probably play an important part. We have reached the stage in our examination of the phenomenon of atelectasis at which we have progressed perhaps about 25 per cent into understanding the various phenomena seen in dogs. We see patchy atelectases develop spontaneously in dogs that have lain under ether anesthesia, and to which nothing else happens for three or four hours or longer. There may be other factors (we do not know what they are) that are essential to the production of atelectasis. We know that even in bronchial plugging there are many factors that enter besides those commonly thought, simply the absorption of air. Strained breathing greatly accelerates the absorption of air, and even when this breathing is controlled there are still other factors that we do not understand, perhaps congestion, perhaps inflammation.

In other words, we have dogs in which everything is controlled, the type of respiration, the type of bronchial plug, the position of it, everything we can possibly lay our hands on, and still we find 100 per cent variation in the occurrence of atelectasis, even in the rate of formation.

The problem is not solved yet; it is complicated, and there is still a lot of work to be done.

Perhaps I have an explanation for Dr. Lilienthal's observation—I say perhaps because I am not able to say it certainly is so. I have found the same thing in dogs. The patchy atelectasis appears when the lung is inflated and disappears readily. On the other hand, we have found that these patches of atelectasis in dogs, if one carefully explores the bronchial tree with fine scissors and runs down, always have a plug. After you have blown them up the plug is still there. How do they blow up? From intercommunication that exists peripherally from free parts of the lung over in the other parts. The blowing up is very simple. I think that perhaps that is an explanation. I still feel that there may be other explanations for some of these phenomena.

Another point I should like to emphasize is the mechanism of cough. Cough depends on what one might call available air in the lung distal to the plug to remove that plug. That is, if there is no air or if the content of air in that imprisoned part of the lung is lower than in any other part of the lung by a considerable degree, the pressures there are smaller than the pressures elsewhere, and the cough is absolutely unable to evacuate the material. The cough must have a battering ram to use, and that battering ram is the available air in the lung that can be expired; the residual air does the cough no good; it cannot be used by the cough. In other words, if a plug has persisted in the bronchial lumen long enough for the absorption of air to occur to an appreciable degree behind it, then the available air has been lost and the cough can no longer expel or be expected to expel the material unless it gets available air as a result of previous deep inspiration around the peripheral connections. We have seen this occur repeatedly in dogs. We have found that after a partial removal of the air, the air is supplied by the next inspiration, and cough is then effectual in removing the material, so we heartily agree with Dr. Lee, Dr. Henderson and others who first apply deep breathing as a means of prevention of atelectasis, to allow the lung to aerate itself behind the plug. Dr. Lee and his co-workers, in their marvelous work on bronchoscopy being done in this city, that of evacuating just one part of the lobe, enter the lobe and free it and allow air to get into the periphery; cough will do the rest. However, do not forget that cough is not the only actor; ciliary action and peristalsis are also concerned. You cannot depend very much on peristalsis, but ciliary action is known to be effectual.

Dr. Myerson of Brooklyn has observed blood stains carried from the carina to the larynx in twelve minutes. More recently, Dr. Buloway has observed the same thing in the bronchi by roentgenograms, opaque bodies being carried appreciable distances in a few minutes. He calls the action bronchial peristaltic action. I should say that perhaps it was bronchial peristaltic action and perhaps ciliary action. Most patients get well if nothing is done for them. Ciliary action perhaps gets rid of the material; the patients do not have to cough to get rid of it.

DR. POL N. CORYLLOS: Dr. Van Allen and his collaborators presented a thorough experimental paper. The passage of air through the interalveolar septums is a fact of great physiologic importance. I do not think, however, that one needs to consider the alveolar "pores" necessary in the physiology of the gas exchange in the lung. In our paper, Dr. Birnbaum and I discussed this point, which

had already been mentioned in a previous paper of Drs. Van Allen and Adams. The interalveolar "holes" ("trous d'usure," Letulle) were known and carefully studied a long time ago. The question of their existence has been the topic of heated debate among different investigators. The majority tend to believe that the pores generally occur in the lungs of elderly subjects and that they are the result of a wear and tear process. Whatever they may be, these pores are not essential for the explanation of this phenomenon because the interalveolar septums are perfectly permeable to gases. This can be shown by insufflating 100 per cent ether vapor into the alveoli through the obstructing cannula. The passage of air ceases immediately because of the edema of the interalveolar septums caused by the ether. This explains why patchy atelectasis is possible only in the presence of some degree of inflammatory edema of the alveolar endothelium. In a healthy lung patchy atelectasis would be little short of impossible because exchange of gases continues through the interalveolar septums even when an alveolar duct is completely obstructed.

Dr. C. M. Van Allen, New Haven, Conn.: In answer to the question on lobular atelectasis, I should have gone into that question because it is easily explained. In speaking of the position of the plug of the obstruction, we have spoken of lobular and lobar simply to try to make it simple, but what we really mean is, is the obstruction an isolating obstruction or is it a nonisolating obstruction? An isolating obstruction may be a lobar obstruction or it may be a lobular obstruction in which there is no action of the intercommunicating cores between the two parts of the lung. That may occur readily. We found that these connections between the lobules of the lung function only if a person is breathing normally and deeply; for instance, in a dog that is lying quietly under ether anesthesia, part of the alveoli may be functionless. It is part of nature's method of giving him a margin of safety in his lung. He has too many alveoli for quiet breathing, and after having instituted an obstruction, in such an animal, we find that at first there is no passage of air around through the connections, but if the dog then takes a deep breath spontaneously, as they sometimes do after waking after ether and start to breathe deeply, the connections open up, and after that there is free passage of air. Not only physiologic collapse, but exudate, small pneumonic patches, may interfere with such communication from lobule to lobule. If water is injected into the free parts of the lung, the intercommunications can be plugged up, edema in the lung being a common result, associated with the infection that gives rise to bronchial obstruction.

Any of these various factors may interfere with the action of the intercommunications. We are not saying that they operate under all and every circumstance; they operate in a normal lung when the patient is breathing normally and deeply, and therefore we advocate deep breathing for these patients to maintain the patency of the free parts of the lung.

The other point Dr. Coryllos made was that he could not repeat my experiments. I can explain that also, I believe. He uses a balloon which when inflated thoroughly seals off the bronchial tree, but in inflation, because of the elasticity of the rubber, it spreads itself along the bronchial lumen for quite a distance and therefore not a lobular but a lobar obstruction has been produced. The balloon spreads itself out over the whole bronchus, so that probably no free passages are left there. I wish that he would get one of my cannulas, which selectively obstruct a given point in a bronchial tree, allowing the bronchial branches proximal to that to remain patent, whereas his balloon spreads itself out a long way over the bronchus.

DR. F. T. LORD, Boston: I should like to discuss somewhat further the etiology of atelectasis, because running through the meeting this morning is a current of apparent belief that bronchial obstruction is the only cause of this condition, and I cannot believe that the evidence warrants such an assumption. It has long been recognized that there is a type of atelectasis, retraction or compression atelectasis, arising in consequence of encroachment on pulmonary tissue, most commonly observed in connection with the accumulation of fluid or gas in the pleural sac or under the elevated diaphragm. There is no reason to believe that this type of atelectasis is due to bronchial occlusion. The degree of collapse is usually in direct proportion to the amount of encroachment and the physical signs, modified by extrapulmonary fluid or air, are those of solidification of the lung with open bronchi.

There is also a second well established type, obstruction atelectasis, arising in consequence of bronchial occlusion. With this type, the physical signs are dulness, diminished or absent breathing, voice, whisper and tactile fremitus over the involved region, and this combination of signs is quite different from those over collapsed areas with open bronchi.

In our experience, much reliance can be placed on physical signs in the distinction between collapse with open and collapse with closed bronchi. Roentgen examination, though of value for the establishment of atelectasis, cannot often be expected to afford evidence regarding the presence or absence of bronchial obstruction, and even bronchoscopy may fail definitely to answer the question regarding the ingress and egress of air.

Such considerations are of practical importance in the diagnosis of the condition under discussion and have a bearing on the relation of bronchostenosis to lobar pneumonia, during which, to judge from physical signs, the bronchi are usually open. At times, however, with lobar pneumonia and more often with postoperative pneumonia, there is atelectasis with signs of closed bronchus.

It may be that atelectasis arises only under these two conditions, but there is a small puzzling group in which atelectasis complicates pneumonia or infarction, and at autopsy there is no compression from without, or bronchial occlusion. In such cases it is difficult to exclude the previous presence of a bronchial plug and the persistence of the collapse of the lung after its disappearance, but it may be that a profound disturbance of local function is also capable of causing atelectasis.

DR. POL N. CORYLLOS: Two points have been raised in the discussion of our paper on which I should like to insist. The first is that we should separate "obstructive" from "compressive" atelectasis, and that the latter, "following open or tension pneumothorax or presence of fluid in the pleura, is not produced by the same mechanism." I cannot agree with Dr. Lord on this point. On the contrary, I believe that, although it might seem paradoxic at first sight, the mechanism of production of atelectasis is always the same, namely, bronchial obstruction and absorption of the entrapped alveolar air by the alveolar blood. The factor of the obstruction, although less evident in the compressive than in the obstructive form of atelectasis, is none the less present. In fact, the big bronchi may be patent, but the small bronchioli, artria and ducti alveolares are collapsed. The proof of it is that the simply collapsed but not yet atelectatic lung, as in open pneumothorax, still contains air, and if thrown into water, floats. This shows that notwithstanding the perfect elasticity of the lung, air cannot be completely expelled but it is entrapped in the alveoli because of the collapse and obstruction of the bronchioli. Furthermore, the collapsed lung, which at the time of the production of the open pneumothorax was not airless (not apneumatic

or atelectatic), will become so if the animal survives for the period necessary for the subsequent absorption of the entrapped alveolar air by the mere play of exchanges of gases. Therefore, in compressive as well as in obstructive atelectasis, apneumatosis is produced by exactly the same mechanism.

The second point is that in some cases atelectasis could be produced by bronchoconstriction, as maintained by Dr. Lilienthal. It is, I think, the only point with which I regret to have to disagree with the pioneer of thoracic surgery in this country. I disagree because, as I have already explained, bronchial spasm never produces complete obstruction. In bronchostenosis of any origin, on deep inspiration, when the lung expands and the bronchioli dilate, air enters the alveoli; whereas on expiration, and especially in forced expiratory movement, when the lung and bronchioli collapse, no air can be expelled (one-way valve). Starling and Jackson have given a clear description of the phenomenon. This is why in all instances in which bronchiospasm occurs emphysema and not atelectasis is produced. In allergic asthma in man, anaphylactic shock in the guinea-pig (in which the shock organ is the lung) and in some cases of incomplete bronchial obstruction by foreign body, there is always emphysema and never atelectasis. Furthermore, how can bronchospasm, which is always generalized, explain the lobar distribution of atelectasis and its predilection for the lower lobes or for the lung of the side on which the patient lies? That bronchospasm could be a condition favoring the production of a subsequent complete bronchial obstruction, I would be ready to admit. But even then, why is atelectasis so rare in allergic bronchoconstriction? Wilmer and Lee have lately upheld the thesis that atelectasis is due to allergic bronchiospasm. I am afraid that this way we have unnecessarily complicated the question of atelectasis. I think our society will render a real service to the medical profession if we definitely state that atelectasis is always due to bronchial obstruction. The physician should give the patient the benefit of a careful examination, roentgenographic and bronchoscopic. I am convinced that in this way many patients with latent foreign bodies, early tumors, abscesses of the lung or inflammatory bronchiectasis would be treated accordingly.

AIR IN THE PERITONEAL CAVITY

ITS EFFECT ON THE POSITION AND ACTIVITY OF THE DIAPHRAGM *

RICHARD H. OVERHOLT, M.D.
PHILADELPHIA

That pulmonary hypoventilation exists after abdominal operation is a well accepted fact. The alteration in the type of respiration, the limitation of respiratory effort and the sense of thoracic oppression which many of these patients exhibit or complain of are evidence of this fact. Furthermore, a reduction in the vital capacity of patients after abdominal operations has been demonstrated by Churchill and McNeil,[1] Head,[2] Powers,[3] and Muller, Overholt and Pendergrass.[4] This hypoventilation occurs after lower, as well as after upper, abdominal operations, but is more marked after the latter. It may result from several factors. Last year Muller, Pendergrass and I [4] reported some observations on the pulmonary status of patients before and after abdominal operations. During this study we observed that postoperatively there occurred an elevation of the diaphragm and a restriction of its activity. Recently Patey [5] also observed a diminution in the movements of the diaphragm after abdominal operations. A comparison of the preoperative and postoperative roentgenograms in his paper shows the diaphragm to be elevated at the time of the postoperative examination. The present studies were undertaken in an effort to ascertain what effect the entrance of air, with the resulting alternation of intraperitoneal pressure, had in this process. I have not found any discussion of the problem of disturbed pressure relationships

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beneath the diaphragm resulting from the production of a pneumoperitoneum as a factor in the alteration of diaphragmatic position and activity.

That the intraperitoneal pressure in the upper part of the abdomen is subatmospheric has been observed by Keppich,[6] Melchior and Melchior,[7] Wagoner [8] and Krause.[9] I investigated this subject [10] in dogs, using various methods for recording the pressure, and was able to demonstrate a mean subatmospheric pressure in the epigastrium of all animals in the horizontal or head-up position when breathing was quiet. I found that when the closed method for estimating pressures is used, the intraperitoneal pressure decreases during inspiration and increases during expiration. This is contrary to the observation of others who have used an open system. In other words, the subdiaphragmatic and intrapleural pressures fluctuate in the same direction during respiration, and not inversely, as had previously been reported. This would suggest that, normally, free diaphragmatic activity is favored by a subatmospheric pressure in the upper part of the abdomen. It would obviously be more difficult for the diaphragm to contract against a positive intraperitoneal pressure.

METHOD

Dogs were used in all of these experiments. They were kept under sodium iso-amyl-ethyl barbituric acid anesthesia throughout the period of the experiment. The drug was given intraperitoneally and in a sufficient amount to drop the respiratory rate to 8 to 10 per minute, the usual dose being 50 mg. per kilogram. The position of the diaphragm was determined by making roentgenographic examinations at a uniform distance and exposure with the animal in the horizontal position (fig. 1). It was found that the position and contour of the diaphragm could be ascertained more exactly when the exposures were made laterally. A metal pin was inserted into the intraspinous ligament near the level of the dome of the diaphragm in order to provide a fixed point from which to make measurements. Roentgenograms were made during both inspiration and expiration. Errors in the timing of the exposure were minimized by reducing the respiratory rate and by making the exposure in three-twentieths of a second.

In order to check up on the accuracy of this method for determining diaphragmatic position, control animals under sodium iso-amyl-ethyl barbituric acid anesthesia were examined at different times on different days during the

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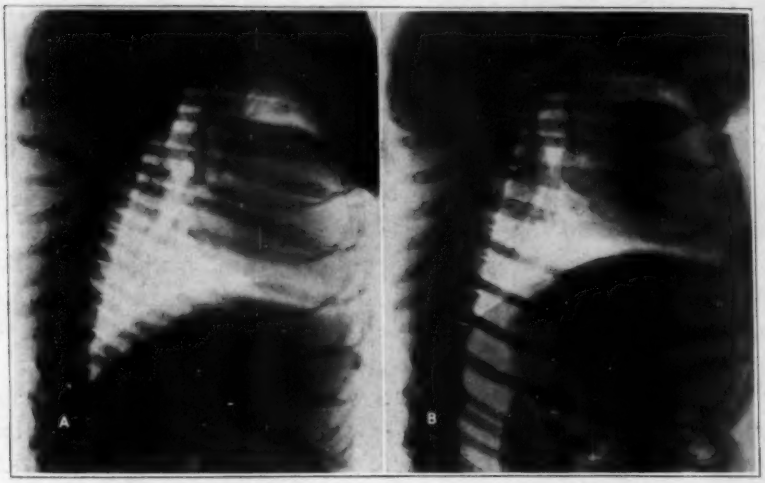

Fig. 1.—Lateral roentgenograms made before (*A*) and after (*B*) laparotomy on dog weighing 10 Kg., with uniform position, distance, exposure and respiratory phase. Illustrates method of studying position of diaphragm. Notice clearcut diaphragmatic shadow throughout. Metal marker and thoracic vertebra used as fixed points in making tracings. Elevation after laparotomy was 1.7 cm. Diaphragmatic excursion before laparotomy was 1.2 cm., and after laparotomy, 0.6 cm.

Fig. 2.—Superimposed tracings made from roentgenograms of two of the control animals. These experiments test the accuracy of the method of measuring changes in the position of the diaphragm. At left, superimposed tracings of roentgenograms made on the same animal on different days, the exposure being made during inspiration. At right, tracings made one hour apart, both exposures during expiration. Note the similarity of these tracings.

same phase of respiration. Tracings made of these roentgenograms and superimposed on each other showed the diaphragm to be in approximately the same position in each exposure (fig. 2). No animals were used in these experiments in which the breathing was fast and difficult to follow. Often several roentgenograms were taken during the same phase of respiration in order to check the accuracy of the timing.

In seventeen animals pneumoperitoneum was induced by injecting air in amounts varying from 10 to 100 cc. per kilogram of body weight. In seven animals, studies were made before and after a laparotomy had been performed. Diaphragmatic position and the extent of diaphragmatic excursions were determined by superimposing tracings of the roentgenograms made during inspiration and expiration before and after the pneumoperitoneum had been induced.

Changes in the movements of the diaphragm were observed fluoroscopically and recorded in eight animals before and after the injection of air into the

Fig. 3.—Kymographic tracing showing the effect of the injection of 100 cc. of air (10 cc. per kilogram) at two different times on the character of thoracic and abdominal respiratory movements. Note that the increase in the rate lasted for only three or four minutes.

peritoneal cavity. In three animals, after the injection of air, the fluoroscopic examinations were repeated every forty-five minutes for a period of three hours.

In five animals kymographic tracings of abdominal and thoracic respiratory excursions were recorded before, during and after the injection of air into the peritoneal cavity. Immediately following the injection of air, the respiratory rate increased for a short interval and then dropped back to, or nearly to, its previous rate. This effect is shown in figure 3. For this reason, all roentgenographic studies were delayed until after the respiratory rate had returned to its original level.

RESULTS

Following the injection of air into the peritoneal cavity, or after laparotomy, two changes in the diaphragm were observed. In every animal studied an elevation and a diminution in diaphragmatic excursions were noted.

Fig. 4.—Superimposed tracings of roentgenograms of two animals made during expiration before (solid line) and after (dotted line) 50 cc. of air per kilogram had been injected intraperitoneally. Note change in position of diaphragm, thoracic cage and heart.

Fig. 5.—Superimposed tracings of roentgenograms made during inspiration in two dogs before (solid line) and after (dotted line) a laparotomy had been performed. Note changes in position of diaphragm and also similarity to changes induced by injection of air as shown in figure 4.

Fig. 6.—Superimposed tracings of roentgenograms made during the same phase of respiration before and after laparotomy. Solid line indicates outline of thorax before operation; dotted line, outline of thorax after operation.

The upward shift of the diaphragm could be easily demonstrated when the preoperative and postoperative films made during similar phases of respiration were compared. The degree of the elevation varied from 0.3 to 1.8 cm., the average for the animals given the injec-

Fig. 7.—Superimposed tracings of roentgenograms made during both phases of respiration both before and after laparotomy. Solid line indicates position of diaphragm during expiration, dotted line position during inspiration. Note the extent of diaphragmatic movement before, and the limitation after. Iso-amyl-ethyl barbituric acid anesthesia was used.

TABLE 1.—*Diaphragmatic Elevation in Twenty-One Dogs (Average Weight, 6.7 Kg.) Under Iso-Amyl-Ethyl Barbituric Acid Anesthesia*

	Number of Animals	Elevation, Cm.		
		Inspiratory Phase	Expiratory Phase	Average
After laparotomy	7	0.98	1.1	1.02
After pneumoperitoneum	14	1.4	1.4	0.96

TABLE 2.—*Diaphragmatic Movement in Fifteen Dogs (Average Weight, 8.6 Kg.) Under Iso-Amyl-Ethyl Barbituric Acid Anesthesia*

	Cm.
Normal excursion (6 animals)	1.3
After laparotomy	0.57
Normal excursion (9 animals)	0.69
After pneumoperitoneum	0.35

tion being 0.958 cm., and that for the animals undergoing laparotomy, 1.02 cm. The extent of the elevation depended more on the size of the animal than on the amount of air injected per kilogram of body weight; e. g., after the intraperitoneal introduction of 100 cc. of air per kilogram the diaphragmatic elevation during expiration for a dog weighing 3.5 Kg. was 0.4 cm., whereas in an animal weighing 6 Kg. the elevation was 1.6 cm.

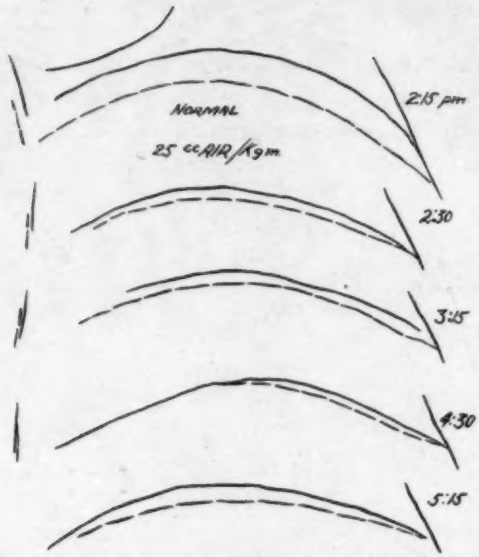

Fig. 8.—Tracings made on the fluoroscopic screen of diaphragmatic excursion before, and at intervals of forty-five minutes after the intraperitoneal injection of 25 cc. of air per kilogram. Solid line indicates diaphragmatic position during expiration; dotted line, position during inspiration. Note definite limitation of excursion of diaphragm which was maintained over a considerable period of time.

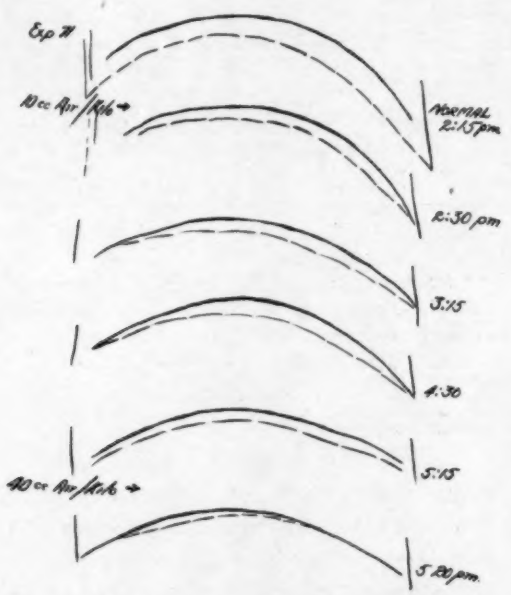

Fig. 9.—Tracings from fluoroscopic screen of diaphragmatic movements under normal conditions and after the intraperitoneal injection of 10 cc. of air per kilogram. Solid line indicates diaphragmatic position during expiration; dotted line, position during inspiration. The reduction of the excursions is noticeable. At the conclusion of the experiment, 40 cc. more air per kilogram was injected, and the diaphragmatic action was further restricted.

The greatest change in the position of the diaphragm took place in the posterior portion. The triangle formed by the border of the heart and the posterior costophrenic angle was diminished in size. The outlines of the bronchi in this area were changed by the retraction of the lung following elevation of the diaphragm. An increase in the size of the thoracic cage was noted; the heart assumed a higher position, and its axis was slightly altered in all of the animals studied (figs. 4 and 5).

A reduction in the extent of the diaphragmatic excursion in animals under iso-amyl-ethyl barbituric acid anesthesia was noted in each instance after the production of a pneumoperitoneum (fig. 6). Under the fluoroscope, injections of from 10 to 100 cc. of air per kilogram caused approximately a 50 per cent decrease in the amplitude of the excursion (figs. 7 and 8). This effect was noted over a period of three hours. After laparotomy in every animal a similar reduction in movement was demonstrated.

COMMENT

These observations indicate that the entrance of air into the peritoneal cavity may be responsible in part for the reduction of pulmonary ventilation by causing elevation and partial limitation of the motion of the diaphragm. The alteration of position and the restriction of activity of the diaphragm may be the result of a change in the intraperitoneal pressure. Under these conditions the diaphragm must move between a positive intraperitoneal and a subatmospheric or negative intrapleural pressure. That the normal pressure relationships in which the diaphragm functions are disturbed after the sealed intraperitoneal space is opened is suggested by the similarity of the results in the injection and laparotomy series. Furthermore, once it has been established that the mean intraperitoneal pressure in the upper part of the abdomen is subatmospheric, it is obvious that an opening of this sealed cavity would cause a change in the pressure in the subdiaphragmatic region.

Two explanations for the fact that variations in the amount of air injected failed to show corresponding elevations in the diaphragm can be given. 1. In previously reported work,[10] it was shown that the intraperitoneal pressure changes immediately from a subatmospheric level to a positive level following small injections of air, but fails to show a corresponding rise on further injections because of the elasticity of the abdominal musculature. This was also pointed out by Coombs[11] in observations on animals after intraperitoneal injections of saline solu-

11. Coombs, H. C.: The Mechanism of the Regulation of Intra-Abdominal Pressure, Am. J. Physiol. **61**:159, 1920.

tion. 2. The structural limitations of the diaphragm itself and the attachment to the costal arch tend to prevent elevation of the diaphragm.

No attempt has been made to attribute all of the diaphragmatic restriction after laparotomy to the presence of air in the peritoneal cavity. It is realized that pain at the site of operation, reflex splinting of the abdominal musculature, distention of the bowel and the application of abdominal binders or dressings also play a rôle in this process.

CONCLUSIONS

The position and mobility of the diaphragm were studied in animals under sodium iso-amyl-ethyl barbituric acid anesthesia. It was observed that following the introduction of air into the peritoneal cavity, either by injection or as a result of laparotomy, the diaphragm assumed a higher position and its excursions were definitely restricted.

Dr. V. C. Johnson of the Department of Roentgenology of the Hospital of the University of Pennsylvania assisted in the fluoroscopic work in this study.

ESOPHAGUS, STOMACH AND HEART FOLLOWING UNILATERAL PHRENICECTOMY*

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That phrenicectomy has a place in the treatment for certain diseases of the lungs would appear to be a more or less accepted fact. In the past, practically all observations in this connection have dealt with the immediate or remote effects of phrenicectomy on a diseased portion of the lung and on the lung as a whole; and justly so, for this is undoubtedly the chief consideration.

We observed gastro-intestinal symptoms in a few patients following phrenicectomy. In one instance the so-called condition of "cardiospasm" supposedly developed following this procedure. We therefore deemed it advisable to study the relationship of the diaphragm to the esophagus both before and after phrenicectomy. The occurrence of certain cardiac symptoms in some of these patients following phrenicectomy also led us to make electrocardiograms before and after the operation.

We have divided our paper into three parts, the first dealing with changes in the esophagus of patients following phrenicectomy, the second with changes in the esophagus of dogs following phrenicectomy, and the third with the electrocardiogram of patients before and after phrenicectomy. The clinical observations were all made on patients in the chest service of Barnes Hospital.

ANATOMIC RELATIONSHIPS OF THE ESOPHAGUS TO THE DIAPHRAGM

The anatomy of the lower end of the esophagus has been thoroughly studied by Mosher [1] and by Mosher and McGregor.[2] Particular atten-

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1. Mosher, H. P.: Liver Tunnel and Cardiospasm, Laryngoscope **32**:348, 1922; Cardiospasm, Pennsylvania M. J. **26**:240, 1923; Findings with the Barium Bougie in Cardiospasm, Ann. Otol., Rhin. & Laryng. **36**:1127, 1927; The Lower End of the Oesophagus at Birth and in the Adult, J. Laryng. & Otol. **45**:161 (March) 1930.

2. Mosher, H. P., and McGregor, G. W.: Study of Lower End of the Oesophagus, Ann. Otol., Rhin. & Laryng. **37**:12 (March) 1928; Study of Lower End of Oesophagus, Tr. Am. Laryng., Rhin. & Otol. Soc. **34**:294, 1928.

tion has been paid to the crural fibers and to their formation of a muscular sling about the lower end of the esophagus. The diaphragm, which is a dome-shaped musculomembranous sheet, receives its motor innervation from the phrenic nerves. The sympathetic fibers to the diaphragm are tropic while the vagus takes no part in its innervation. The intercostals send sensory fibers to the diaphragm.[3] The esophagus pierces the diaphragm by passing through the muscular hiatus esophagus. It runs obliquely to the left as it passes through the hiatus at the level of the tenth dorsal vertebra and thence continues very obliquely to the left into the stomach. The abdominal portion of the esophagus or epicardia is from about 2 to 5 cm. in length (Carman,[4] Imperatori[5]). Physiologic narrowing of the lower part of the esophagus occurs at the hiatus and at the cardiac opening. Much attention has been directed to these two points in discussions on "cardiospasm."

The structure and position of the diaphragmatic crura seem to constitute a perfect mechanism for pinching shut the esophagus at this point. Jackson[6] suggested that the barrier to regurgitation which can automatically open at the approach of a bolus of food is located at the diaphragm and is due to two mechanisms: (1) the normal kinking of the abdominal part of the esophagus, and (2) the diaphragmatic pinchcock. Joannides[7] observed two types of contraction in the lower part of the esophagus of the anesthetized dog. By inserting a finger into the esophagus through a gastrostomy opening he could produce a circular constricting "esophageal" contraction as a result of stimulation of the peripheral end of the vagus or of the esophagus at any level above the gastro-esophageal junction. A second type of contraction was coincident with each inspiration and was apparently due to contractions of the diaphragmatic pillars. This "milking action" was also observed following stimulation of the trunk or branches of the phrenic nerve in the immediate vicinity of the pillars. Sauerbruch[8] noted that the resistance felt by a finger introduced into the esophagus through a gas-

3. Kiss, F., and Ballon, H. C.: Contribution to the Nerve Supply of the Diaphragm, Anat. Rec. **41**:285 (Feb. 25) 1929.

4. Carman, Russell D.: The Roentgen Diagnosis of Diseases of the Alimentary Canal, ed. 2, Philadelphia, W. B. Saunders Company, 1920.

5. Imperatori, C. J.: Cardiospasm, Arch. Otolaryng. **11**:178 (Feb.) 1930.

6. Jackson, Chevalier: The Diaphragmatic Pinchcock in So-Called "Cardiospasm," Laryngoscope **32**:139, 1922.

7. Joannides, M.: Influence of the Diaphragm on the Esophagus and on the Stomach, Arch. Int. Med. **44**:856 (Dec.) 1929; The Relation of the Hiatus Oesophageus of the Diaphragm to the Stomach, ibid. **43**:61, 1929.

8. Sauerbruch, F.: Chirurgie der Brustorgane, Berlin, Julius Springer, 1925, vol. 2. Sauerbruch, F., and Haecker, R.: Zur Frage des Cardiaverschluss der Speiseröhre, Deutsche med. Wchnschr., Aug. 2, 1906, no. 3.

trostomy opening and attributed by him to the sling of the diaphragm disappeared following section of both phrenic nerves.

It is obvious from such experiments that there exists a close relationship between the normal diaphragm and esophagus. It is therefore of interest to determine the effect of a high insufficient diaphragm on this relationship.

EFFECTS OF INSUFFICIENCY OF THE DIAPHRAGM

Following phrenicectomy the diaphragm on the same side becomes paralyzed, atrophic and elevated and usually shows a paradoxic movement on respiration. Conditions similar in every respect have been found in certain cases of eventration or "insufficiency" of the diaphragm. It is therefore advisable to consider cases of eventration.

Lerche [9] advised the term "insufficiency" rather than eventration for the condition in which an abnormally high leaf of the diaphragm, usually the left, forms a saclike dilatation into which one or more of the abdominal organs, especially the stomach, colon or even the spleen, are displaced upward. The various causes ascribed to this condition are: congenital atrophy, dystrophy, neuromuscular degeneration following injury, neuritis or other involvement of the phrenic nerve or its fibers, certain infectious diseases and changes in the musculature of the diaphragm such as pseudohypertrophic lipomatosis and myositis.

Acute insufficiency of the diaphragm has been observed following one of the infectious diseases. After a few weeks the diaphragm returns to its normal level, and all symptoms disappear.[9]

Chronic insufficiency of the diaphragm includes those cases in which there is a permanently elevated diaphragm. Patients with this condition may be singularly free from symptoms for a considerable period.[9] They may, however, have sensations of heaviness in the epigastrium and may also be troubled with dysphagia or gaseous eructations (Dillon [10]). They may also complain of dyspnea on exertion. In such cases of eventration one finds a permanently large stomach bubble under the highly arched diaphragm which may even be at the level of the third interspace.

Hitzenberger [11] stated that in the case of a high left diaphragm the pars cardiaca is displaced upward and dorsally, the lower end of the esophagus craniodorsally instead of caudoventrally. This causes an angulation of the esophagus which he believed may be responsible for

9. Lerche, W.: Insufficiency (Eventration) of the Diaphragm, Surg. Gynec. Obst. **34**:224, 1922.

10. Dillon, J.: Die Beziehungen zwischen Zwerchfellfunktion und Verdauungskrankheiten, Arch. f. Verdauungskr. **42**:685, 1928.

11. Hitzenberger, K.: Das Zwerchfell, Vienna, Julius Springer, 1927.

the so-called "dysphagia paradoxa." It is called paradoxic dysphagia, because such patients are able to swallow solids better than liquids, and because they fail to lose weight. Eppinger [12] stated that in the case of a diaphragm high on the left side the greater curvature of the stomach comes to lie anteriorly and superiorly while the lesser curvature lies inferiorly and posteriorly. The duodenum is also displaced. Lerche [9] reported somewhat similar observations in a case of eventration of the diaphragm. There was angulation of the abdominal portion of the esophagus as it entered the elevated cardia and rotation of the stomach so that the greater curvature pointed directly forward. Esophagoscopic examination in this instance confirmed the observation of increased angulation of the abdominal part of the esophagus to the left. The patient swallowed a tube filled with barium sulphate. Under the fluoroscope it was observed that the esophagus turned upward into the fundus at a more acute angle than is usually seen.

Hitzenberger [11] also stated that in the case of a diaphragm high on the right side the pylorus may come to occupy such a position as to make the longitudinal axis of the stomach lie transversely.

Such definitely disturbed relationships between the esophagus and the stomach in cases of eventration of the diaphragm warrant even more careful consideration of the effects of phrenicectomy.

LITERATURE NOTING GASTRO-INTESTINAL SYMPTOMS FOLLOWING PHRENICECTOMY

Hecht [13] noted that some of his patients complained of a feeling of fulness after a large meal the first few days following phrenicectomy. He observed one patient with such complaints which persisted for a few weeks following a right-sided phrenicectomy.

Maendl and Schwarzmann [14] reported their experiences in 100 phrenicectomies. Almost all their patients the left side of whose diaphragms were paralyzed suffered from loss of appetite, a feeling of fulness and vomiting directly after the operation, which was performed under local anesthesia.

In reporting 300 phrenicectomies Welles [15] stated that in a small number of cases the rise of the diaphragm was followed by digestive upsets. The majority of these were temporary and were no more common following left-sided than following right-sided phrenicectomy.

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12. Eppinger, K., quoted by Hitzenberger (footnote 11).

13. Hecht, P.: Phrenicusexhirese und gastrokardialen Symptomkomplex, Beitr. z. Klin. d. Tuberk. **70**:336, 1928.

14. Maendl, H., and Schwarzmann, E.: Unsere Erfahrungen bei 100 Phrenicoexairesen, Beitr. z. Klin. d. Tuberk. **71**:80, 1929.

15. Welles, E. S.: Phrenicectomy in Three Hundred Cases of Pulmonary Tuberculosis, Arch. Surg. **19**:1169 (Dec.) 1929.

Uebelhoer [16] reported an example of relaxatio diaphragmatica following a left-sided phrenicectomy on a woman, aged 24, with pulmonary tuberculosis and cavitation. This case was reported in 1928, and the operation was performed in October, 1924. This patient had had some obstipation and vomiting before the operation. These symptoms were markedly increased following the phrenicectomy. There was no cardiac displacement. The patient did not complain of palpitation. The condition after the phrenicectomy suggested either a relaxed diaphragm or a diaphragmatic hernia. Sauerbruch [8] operated on the patient, found a relaxed diaphragm and plicated it; the patient was relieved of her symptoms. The diaphragm was found at the level of the fourth rib. The authors stated that they never observed an elevation of the diaghragm after phrenicectomy above 8 to 9 cm. on the left or above 12 cm. on the right. They stated that the following considerations arose in their case, which is the only one observed in a personal series of 1,000 phrenicectomies: 1. The shrinking lung may have pulled the diaphragm with it, since the wall of the chest and the mediastinum were unyielding because of adhesions. 2. A coexisting meteorism expressive of an increased intra-alimentary pressure forced the diaphragm up higher than usual. This is in accord with the views of Assmann.[17] 3. There may have been a congenital basis, that is, a preexisting weakness of the diaphragm.

THE EFFECT OF PHRENICECTOMY ON THE ESOPHAGUS

We examined twenty-seven patients before and after phrenicectomy. Fluoroscopic and roentgen examinations of the esophagus and stomach with the use of an opaque meal consisting of a thick mixture of barium sulphate and water were made. Five of the twenty-seven patients whom we examined complained of the following symptoms following phrenicectomy: one of eructations of gas, another of "heart burn," a third of vomiting and two of dysphagia. One of the latter symptoms occurred after a right-sided phrenicectomy. Our observations were made on patients who had phrenicectomy performed for pulmonary tuberculosis (nineteen cases), bronchiectasis, chronic abscess of the lung, chronic empyema or hemoptysis.

We have considered our cases as follows:

1. Left-sided phrenicectomies with marked elevation of the paralyzed leaf of the diaphragm.

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16. Uebelhoer, O.: Relaxatio diaphragmatica nach künstliche Zwerchfellähmung, Deutsche Ztschr. f. Chir. **211**:266, 1928.

17. Assmann, H.: Klinische Röntgendiagnostik der inneren Erkrankungen, ed. 4, Leipzig, F. C. W. Vogel, 1929.

2. Left-sided phrenicectomies with slight elevation of the paralyzed leaf.

3. Left-sided phrenicectomies in cases in which there was a large left pneumothorax before, which was maintained following phrenicectomy.

4. Right-sided phrenicectomies.

We observed that the thoracic portion of the esophagus may be deflected to the right or the left because of fibrosis, pleural effusions, pneumothorax or kyphoscoliosis. The degree and acuteness of this deflection and whether or not it will be productive of symptoms are naturally dependent on the site and nature of the underlying lesion. Thus localized, mediastinal fibrosis with changes in the lung may affect

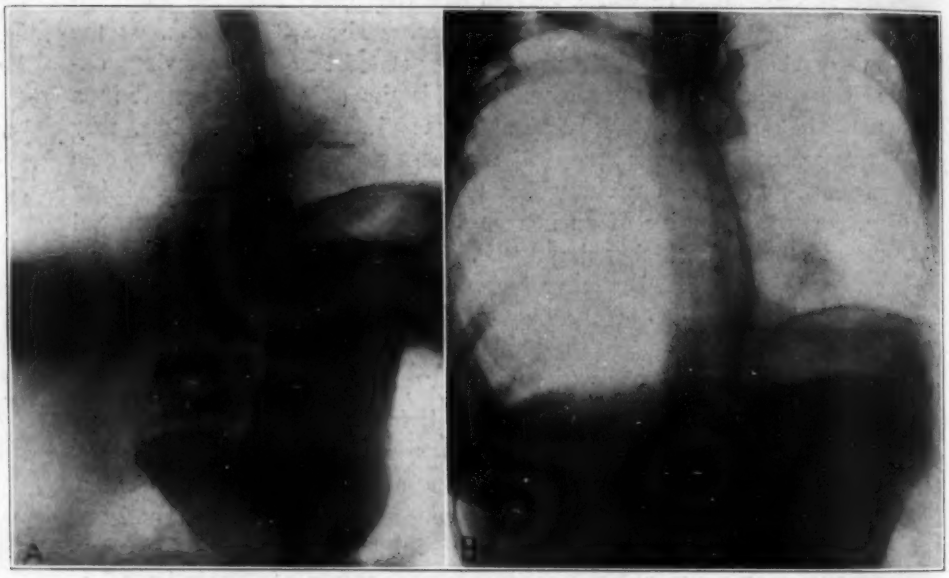

Fig. 1.—A woman, aged 25, with tuberculosis of the left lung: *A*, this film, taken before the phrenicectomy, shows displacement of the thoracic part of the esophagus; the displacement is due to pulmonary fibrosis; *B*, this film, taken after the phrenicectomy had been performed, shows moderate elevation of the left side of the diaphragm. Note the large stomach bubble and the increased angulation of the abdominal portion of the esophagus. The patient was free from gastric symptoms.

the esophagus at only one point. In fact, as already mentioned, the esophagus was sometimes found permanently displaced to the affected side.

Concerning the upper half of the thoracic portion of the esophagus, we observed no marked mechanical displacement or shift with respiration following phrenicectomy.

Following phrenicectomy we did observe slight respiratory deflection of the lowermost thoracic portion of the esophagus. The normal contracting leaf of the diaphragm appeared to displace the lower part of the esophagus to the innervated side during inspiration, and permitted it to return to its former position during expiration.

Our chief interest was centered around the abdominal portion of the esophagus and what might happen to it following phrenicectomy. The abdominal portion of the esophagus could be affected in two ways: (1) as a direct consequence of the anatomic rearrangement following the rise in the diaphragm and (2) as a result of the pull of the opposite contracting diaphragm. Both could, of course, operate.

We have observed that elevation of the left side of the diaphragm following phrenicectomy results in upward displacement of the stomach and gives rise to a permanently large stomach bubble. We have noted that the curve that the esophagus normally makes after it leaves the hiatus to enter the stomach can become sharper (fig. 1). Whether the upward displacement of the diaphragm and stomach is due to negative intrathoracic pressure, increased intra-abdominal (or intra-alimentary) pressure or disproportion between the two we do not know. The colon may also come to occupy a position within the thorax. One cannot with absolute certainty say that the stomach and colon follow the diaphragm in a purely passive way. Certainly interposition of other structures between the diaphragm and the stomach is rare.

Fluoroscopic examination of one patient following right-sided phrenicectomy showed that the barium-filled stomach became deflected to the right with each inspiratory contraction of the left side of the diaphragm.

Dr. Sherwood Moore[18] observed that there may be displacement of the pylorus to the left in cases in which the fundus is displaced upward. He therefore suggested that this upward displacement might be due to contraclockwise rotation of the greater curvature, the lesser curvature remaining more or less fixed. This would tend to prevent marked distortion of the abdominal portion of the esophagus which would otherwise occur. He felt that this point requires further confirmation.

Our observations in the cases grouped in the manner previously noted have been as follows:

1. Cases that resulted in a marked elevation of the left diaphragm also showed a very large stomach bubble and increased angulation of the abdominal portion of the esophagus (fig. 2). Such angulation following phrenicectomy is not of serious moment.

18. Moore, Sherwood: Personal communication to the authors.

2. Those cases which resulted in only slight elevation of the left side of the diaphragm failed to show any marked change in the position of the abdominal part of the esophagus (figs. 3 and 4).

3. Those cases in which there was a large left pneumothorax before and after phrenicectomy also showed only moderate elevation of the diaphragm and consequently little or no increased angulation of the abdominal part of the esophagus.

4. We failed to observe any definite permanent change in the abdominal part of the esophagus following right-sided phrenicectomy.

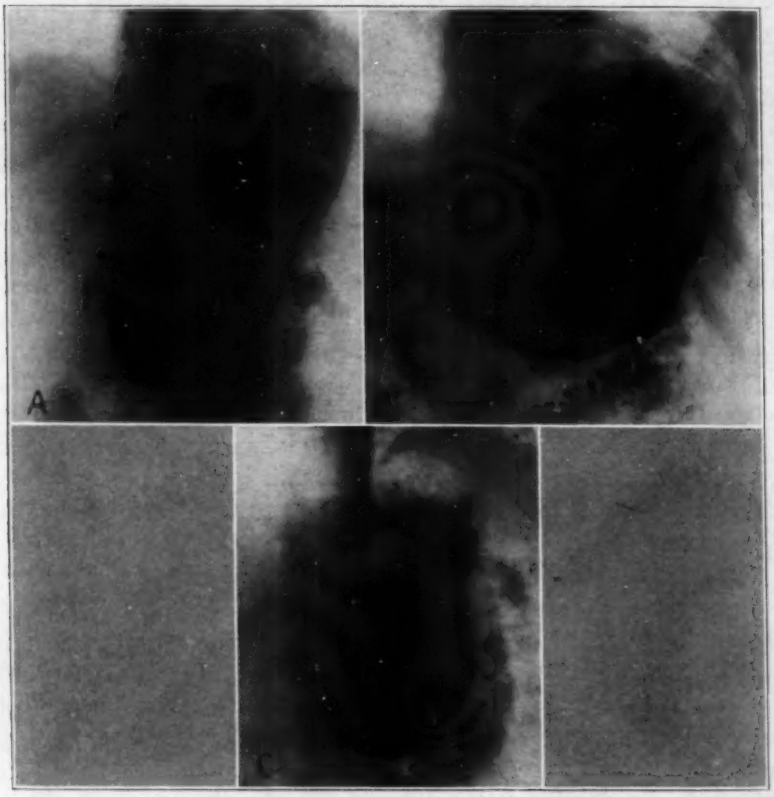

Fig 2.—A man, aged 24, with tuberculosis of the left lung: *A*, this film, taken ten months after phrenicectomy, shows definite elevation of the left side of the diaphragm and a large stomach bubble; *B*, this film, taken with the patient in the recumbent position strongly suggests contraclockwise rotation of the greater curvature of the stomach; *C*, note the marked angulation of the abdominal part of the esophagus. A complete series of roentgenograms of the gastro-intestinal tract showed increased alimentary motility chiefly of the colon but without localization in the cecal portion. The patient was troubled with vomiting.

When the barium mixture is thin there is no delay in the flow from the esophagus to the stomach either before or after phrenicectomy. When a thick paste is used, however, the bolus may be held up in the

esophagus and the normal "milking action" observed; that is, the barium enters the stomach during expiration. During inspiration the flow of barium seems to be interrupted, so that no barium is observed in the esophagus below the diaphragm. This milking action is not impaired following unilateral right-sided or left-sided phrenicectomy. We have not had an opportunity to study the "milking action" in a patient in whom both phrenic nerves were cut. From the experimental work done by Sauerbruch [8] we would expect the milking action to be lost in the case of bilateral phrenicectomy.

Fig. 3.—A man, aged 26, a patient of Dr. Duff Allen, had tuberculosis of the left lung. A left-sided phrenicectomy was performed on Oct. 14, 1929. This film, taken in April, 1930, shows displacement of the thoracic portion of the esophagus which is due to pulmonary and mediastinal fibrosis. The left side of the diaphragm is only moderately elevated. There is a large stomach bubble, but only slight angulation of the abdominal part of the esophagus. The patient began to complain of eructations of gas, six months after the phrenicectomy.

We have failed to observe any marked delay in the emptying of the esophagus following phrenicectomy.

It is obvious that we have endeavored to draw some analogy between an eventrated diaphragm and a high paralyzed diaphragm following phrenicectomy. The etiologic factor may be the same in both, injury or destruction of the phrenic nerve. Histologically the diaphragm in both cases is atrophic. An anatomic rearrangement of the normal

relationship between stomach and esophagus exists in both. We believe that phrenicectomy has been performed so frequently without the production of symptoms that, as in the case of eventration of the diaphragm, perhaps some hitherto unmentioned factor is necessary to precipitate symptoms.

It is difficult to localize the symptoms noted by our patients in any one part of the gastro-intestinal tract. Air which normally collects in the stomach may fail to be expelled readily following phrenicectomy

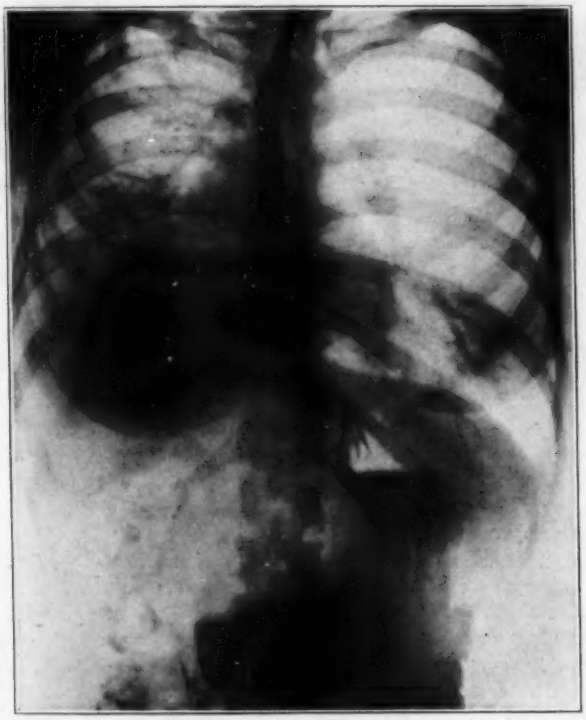

Fig. 4.—A woman, aged 22, a patient of Dr. Duff Allen: A right-sided phrenicectomy was performed for pulmonary tuberculosis. This film shows displacement of the thoracic portion of the esophagus which is the result of pulmonary fibrosis. Fluroscopic and roentgen examination failed to show any increase in the size of the stomach bubble and no increased angulation of the abdominal portion of the esophagus. The normal milking action of the diaphragm could still be observed after the diaphragm had been paralyzed.

because of the loss of the contractile power of the diaphragm. This in itself may be sufficient to produce symptoms.[19]

19. Knosp, J.: Die Therapie des gastrokardialen Symptom Komplexes, Ztschr. Arztliche Fortbildung **15**:720 (Nov.) 1929.

THE APPARENT OCCURRENCE OF "CARDIOSPASM" FOLLOWING PHRENICECTOMY

We observed so-called "dysphagia paradoxa" only in the patient in whom "cardiospasm" developed.

REPORT OF CASE

CASE 1.—A white woman, aged 36, was first admitted to Barnes Hospital on Oct. 23, 1927, with complaints of cough associated with choking and vomiting, expectoration and the loss of 20 pounds (9 Kg.) in weight in two years. The

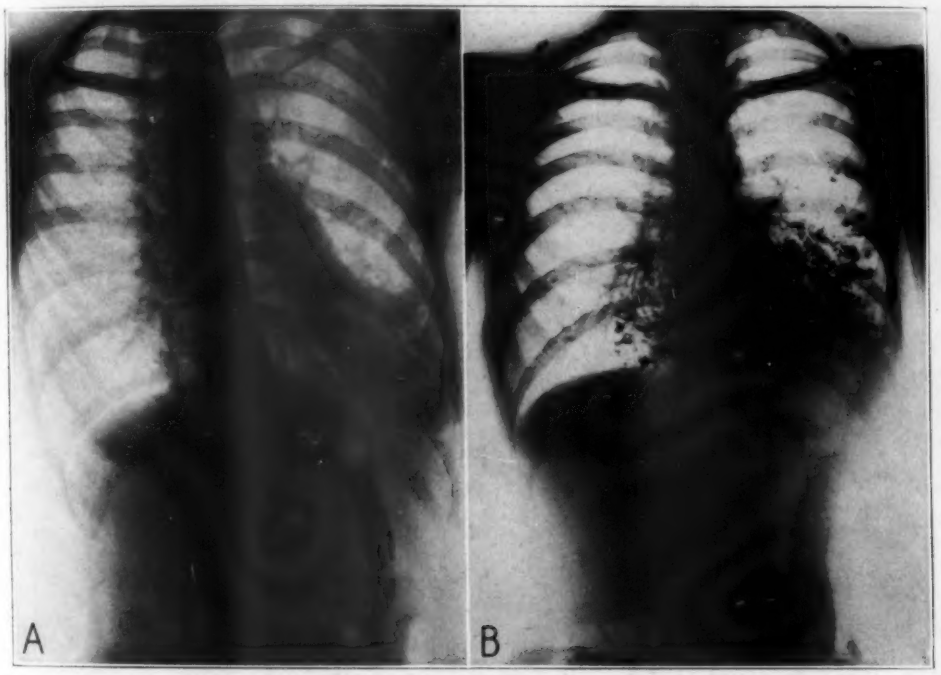

Fig. 5.—A woman, aged 36, with bilateral bronchiectasis: A left-sided phrenicectomy was performed on April 12, 1928. Two months later dysphagia developed. *A*, this film, made during October, 1929, shows an even dilatation of the esophagus, above the diaphragm, and an even, smooth narrowing of the lower extremity of the esophagus; *B*, this film, made two days after an esophagoscopic examination, shows the bronchial tree outlined with iodized oil and the esophagus outlined with barium. The left side of the diaphragm is slightly elevated. There is no marked angulation of the abdominal portion of the esophagus.

patient had had repeated attacks of pneumonia. She had also suffered from constipation and occasional pain in the left lower quadrant.

Her present illness began when she was 6 years of age. Her cough appeared at that time, and from 1907 to 1926 she had recurrent attacks which apparently lasted for a considerable period every winter. Her expectoration was bloody,

foul and rather copious. She also had fever, sweats and chills. Her attacks of coughing occasionally caused vomiting.

On admission her complaints were apparently as severe as they had ever been. Physical examination showed many râles at the base of the left lung. An injection of iodized poppy seed oil 40 per cent (by the aspiration method) demonstrated the presence of bronchiectasis of the lower lobes of the lungs. Examinations of the sputum were repeatedly negative for tubercle bacilli, and the Wassermann reaction was negative. Artificial pneumothorax was attempted, but air could be introduced only in small amounts because of adhesions, so that this treatment was soon discontinued. The patient made some improvement on postural drainage.

A left phrenicectomy was performed by Dr. Graham on April 12, 1928. The patient was discharged from the hospital ten days later. The left side of her diaphragm was paralyzed and definitely elevated.

One and one-half years after the phrenicectomy the patient was readmitted to Barnes Hospital (October, 1929). Her chief complaint was dysphagia. She stated that the difficulty in swallowing developed two months after phrenicectomy. At the time of admission dysphagia was less marked than it had been two months previously. Liquids caused more difficulty than solids, and she occasionally regurgitated undigested food. She also complained of substernal oppression. She had no pain and had not lost weight. A roentgenogram made shortly after admission showed an even dilatation of the esophagus (fig. 5). This dilatation seemed to start a short distance above the diaphragmatic opening of the esophagus. There was an even smooth narrowing of the lower extremity of the esophagus. Dr. Arbuckle made an esophagoscopic examination on Oct. 11, 1929. The patient received ⅙ grain (10.8 mg.) of morphine and $\frac{1}{150}$ grain (0.4 mg.) of atropine thirty minutes before esophagoscopy was performed. No local anesthesia was used, and it is noteworthy that the patient did not gag or show any sign of feeling the tube. The esophagus was found to be filled with frothy mucus from a point just below the cricopharyngeus muscle down to the diaphragm. The mucosa of the esophagus appeared otherwise normal. At the level of the diaphragm the interior of the esophagus resembled an old-fashioned tobacco pouch closed by twisting. The right wall of the esophagus seemed to travel posteriorly, and the left wall anteriorly, in making the twist. The lumen of the esophagus at the level of the diaphragm could be readily dilated to admit the full-sized tube. The stomach appeared normal.

Following esophagoscopy the patient was given atropine sulphate, $\frac{1}{200}$ grain (0.3 mg), twice a day. Fluoroscopy four days later still showed a dilated esophagus, but the flow of barium into the stomach was more prompt, and the patient was symptomatically improved.

PHRENICECTOMY AND CARDIOSPASM

We are forced to comment on the relationship of the diaphragm to "cardiospasm," as we have noted one possible case following phrenicectomy.

Jackson stated that of hundreds of cases of so-called cardiospasm he had never seen any in which the spasm at the hiatus was any greater than what might be called maximum normal. His opinion, based on esophagoscopic observations, is that the failure to open, and not excessive spasm of the diaphragmatic pinchcock, is the chief etiologic factor

in many of the cases of cardiospasm. Rieder [20] noted that the spasm which is felt by one's finger in the esophagus does not disappear if the vagi are cut. It disappears, however, when both phrenic nerves are cut (Sauerbruch [8]). Rieder has never been able to produce cardiospasm experimentally.

Sauerbruch [8] considered the sling of the diaphragm to be all-important in the production of "cardiospasm." Guns [21] pointed out that a phrenospasm may be found in normal subjects, and cardiospasm in patients with esophagectasia. He stated further that at the beginning of an acquired dilatation of the esophagus, a phrenospasm exists. It is later changed into a cardiospasm. It is interesting to note that Birnberg [22] stated that both Douglas and Morrison blocked phrenic nerves of patients with alcohol in an effort to relieve cardiospasm, but without result. Ernst [23] did not observe any obstruction at the cardia in forty-one patients following phrenicectomy.

As symptoms of cardiospasm developed in one patient two months after phrenicectomy, and as we found definite evidence of the condition eighteen months later, it was suggested that cardiospasm might be a consequence of phrenicectomy.

EXPERIMENTS ON ANIMALS

Our experimental investigations were carried out on dogs. The following questions were considered:

1. Is there any obstruction at the lower end of the esophagus following phrenicectomy?
2. Does an elevated diaphragm result in displacement of either the thoracic or the abdominal portion of the esophagus?
3. Does the esophagus become deflected by respiratory movements of the diaphragm on the nonparalyzed side following phrenicectomy?
4. Is the size or shape of the esophagus altered following phrenicectomy?
5. Is there any evidence of so-called "cardiospasm" following phrenicectomy?

Technic.—All our experiments were performed on dogs. In the early experiments the animals were given ether anesthesia. It was soon noted that the esophagus appeared extremely dilated as a result. Anesthesia was therefore not used when the roentgenograms were made. Various means of filling the esophagus with an opaque meal were tried. The best results were obtained by using an

20. Rieder, W.: Der sogennanten Cardiospasmus: Eine experimentelle Studie, Deutsche Ztschr. f. Chir. **217**:334, 1929; Klinik und Therapie des sogenannten Cardiospasmus, ibid. **222**:47, 1930.

21. Guns, P.: Phrenospasm and Cardiospasm in Mega-Esophagus, Arch. Otolaryng. **8**:156 (Aug.) 1928.

22. Birnberg, T. L.: Cardiospasm in the New-Born Infant, Am. J. Dis. Child. **38**:1183 (Dec.) 1929.

23. Ernst, M.: Künstliche Zwerchfellähmung und Cardiospasmus, Deutsche Ztschr. f. Chir. **220**:258 (Nov.) 1929.

ordinary 50 cc. syringe to inject the barium mixture through a rubber catheter, which was introduced into the esophagus through a perforated wooden mouth gag. The catheter was passed into the upper third of the esophagus, so that complete filling of the lower two-thirds was obtained. Roentgenograms were taken immediately following the injection.

The phrenic nerve was severed in the thorax close to the diaphragm. All phrenicectomies were performed under ether anesthesia. The positive pressure machine of Erlanger and Gessel was employed.

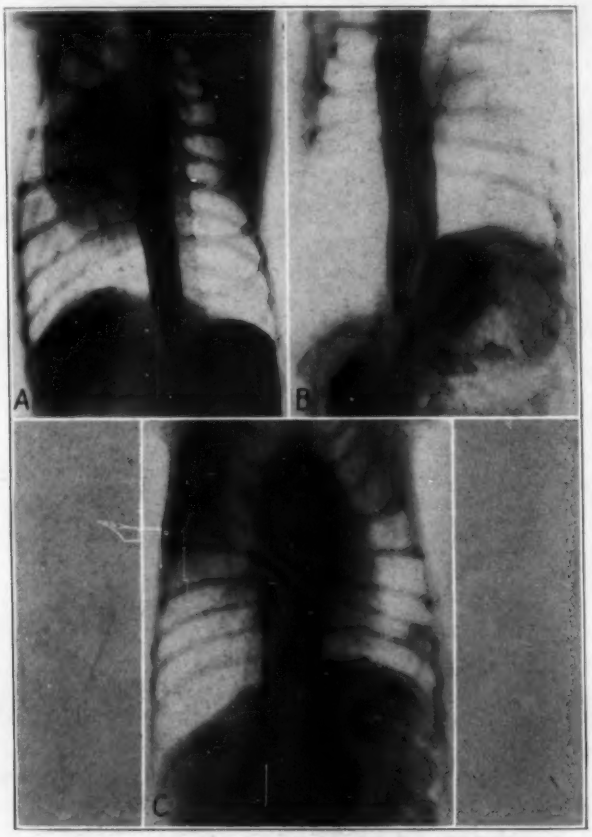

Fig. 6.—Dog 324: *A*, this film, taken in slightly oblique position shows a normal esophagus; *B*, this picture, taken after the phrenicectomy, shows definite elevation of the left side of the diaphragm and increased angulation of the abdominal portion of the esophagus; the fundus of the stomach lies high beneath the elevated left side of the diaphragm; *C*, in this film, taken seven weeks postoperatively; note the dilated esophagus. Barium has not been prevented from entering the stomach.

Left Phrenicectomy: Dog 324.—Control films taken on Dec. 10, 1929, showed a normal esophagus. The left phrenic nerve was cut on the following day. A film taken ten days after the operation showed the left side of the diaphragm

definitely elevated. There seemed to be increased angulation of the abdominal part of the esophagus. This resulted from the ascent of the fundus of the stomach beneath the elevated leaf of the diaphragm. This film was taken in a slightly oblique position so that the barium filled stomach would not overlie the abdominal portion of the esophagus. Definite dilatation of the esophagus was noted in a film taken seven weeks after operation (fig. 6). The animal ate well and did not

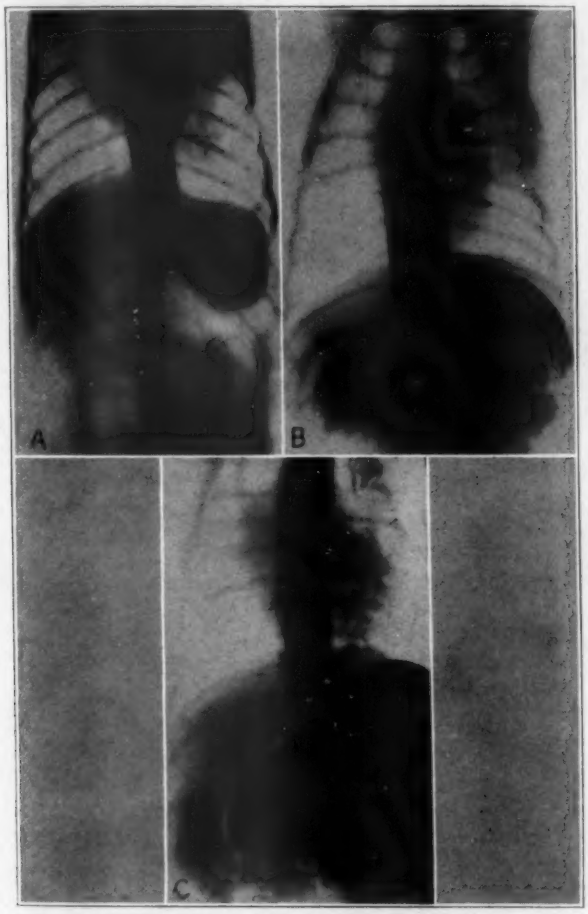

Fig. 7.—Dog B10: *A*, a control film, taken March 28, 1930; *B*, appearance following left-sided phrenicectomy which was performed on April 1; *C*, this film, taken on the eighth postoperative day, shows slight elevation of the left side of the diaphragm with but slight upward displacement of the stomach. Note the double shadow cast by the esophagus. This is due to the fact that both phases of respiration have been registered on the same film. It probably indicates the amount of esophageal displacement by the normal contracting right diaphragm.

lose weight. At no time was there any evidence of obstruction at the cardiac end of the esophagus. This dog was killed by other dogs on March 8, which was the seventy-seventh day after operation. Necropsy showed that the trachea was

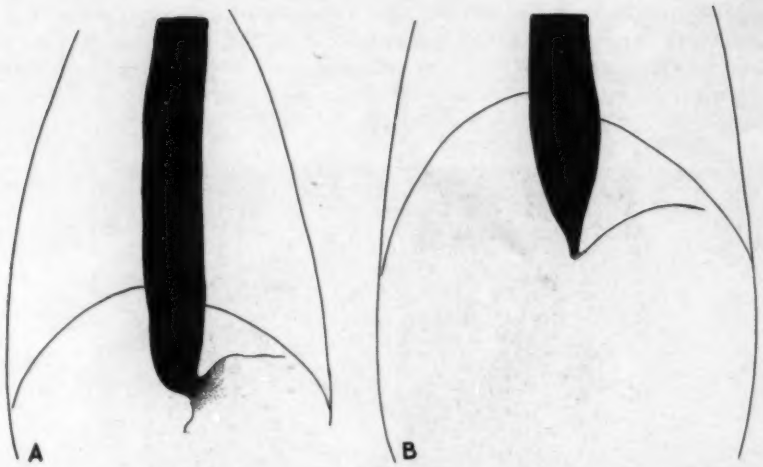

Fig. 8.—Dog 300: *A*, a control film, taken on Dec. 27, 1929; a right-sided phrenicectomy was performed on Jan. 8, 1930; *B*, this film, taken on the twelfth postoperative day, shows elevation of the right side of the diaphragm but no displacement of the abdominal portion of the esophagus or the stomach.

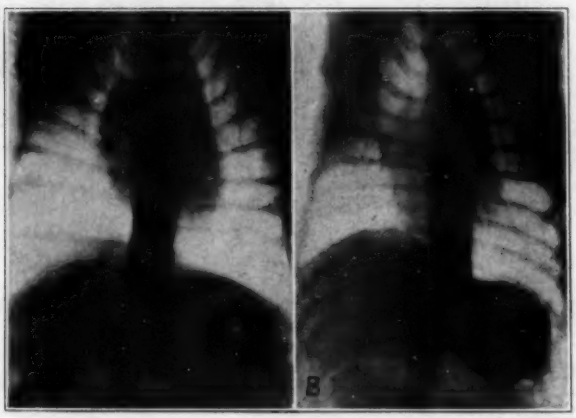

Fig. 9.—Dog 5441: *A*, normal esophagus; *B*, this film shows definite elevation of the right side of the diaphragm. The lower thoracic part of the esophagus is displaced to the left. Barium has entered the stomach. There is no evidence of increased angulation of the abdominal portion of the esophagus and no evidence of obstruction at the lower end of the esophagus.

crushed. The left pleural cavity was clean. There were a few pleural adhesions between the lower lobe of the left lung and the muscularly atrophic elevated diaphragm.

Dog B 10.—Control films, taken on March 28, 1930, showed what appeared to be a normal esophagus. A left-sided phrenicectomy was performed on April 1. A film taken on the eighth postoperative day showed slight elevation of the left

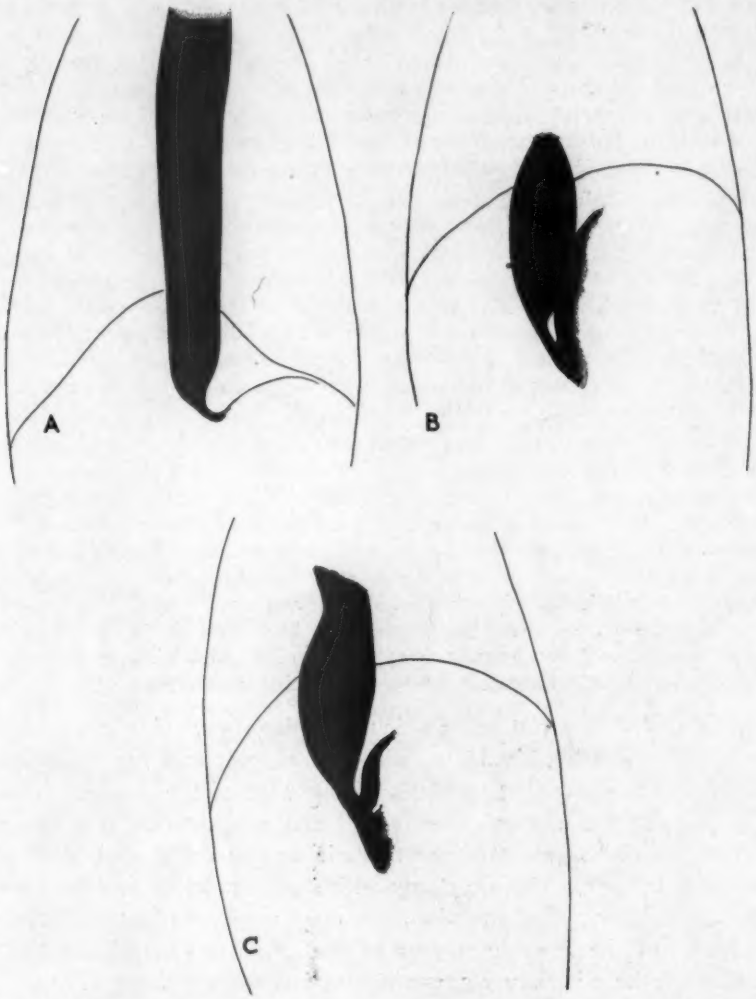

Fig. 10.—Dog. 348: *A*, control film, made on Jan. 8, 1930; *B*, a left-sided phrenicectomy was performed and the diaphragm plicated. This film was taken five days postoperatively. The stomach did not show the upward displacement noted following simple elevation of the left side of the diaphragm. There is no increased angulation of the abdominal portion of the esophagus. *C*, this film, taken twelve days postoperatively, shows no evidence of obstruction at the lower end of the esophagus.

side of the diaphragm with slight displacement of the stomach. This was not sufficient to cause increased angulation of the abdominal portion of the esophagus. Another film taken on the same date during both phases of respiration showed a double shadow of the esophagus, which probably indicates the amount of esophageal displacement by the normally contracting right side of the diaphragm (fig. 7). It should be noted that two films taken on the same date show a wider esophageal shadow in one than in the other. We believe that this was due to overfilling of the esophagus with barium.

Right Phrenicectomy: Dog 300.—Control films were taken on Dec. 27, 1929, and a right-sided phrenicectomy was performed in the manner already described. Films taken at intervals following operation showed elevation of the right side of the diaphragm, but we did not observe any change in the size, shape or position of either the thoracic or the abdominal part of the esophagus (fig. 8).

Dog 5441.—Control films were taken on April 1, 1930, and showed a normal esophagus. A right-sided phrenicectomy was performed on the same day. A roentgenogram taken on the eighth postoperative day showed definite elevation of the right side of the diaphragm. The lower thoracic part of the esophagus was displaced to the left, probably being pulled over by the normal contracting left leaf of the diaphragm. Some of the barium had entered the stomach. There was no evidence of obstruction at the lower end of the esophagus and no increased angulation of the abdominal portion of the esophagus, as had been noted in the case of a diaphragm the left side of which is high (fig. 9).

Left-Sided Phrenicectomy with Plication of the Left Side of the Diaphragm: Dog 348.—A control film showed a normal esophagus. On Feb. 26, 1930, a left-sided phrenicectomy was performed, and the left leaf of the diaphragm was plicated by two purse-string sutures and one row of transverse sutures. Films taken on the fifth postoperative day showed an elevation of the left side of the diaphragm. The stomach failed to follow the rising diaphragm. This may have been due to actual increase in thickness of the diaphragm because of the plication or to unequal elevation of the diaphragm. The lower part of the esophagus was seen to be filled with barium, but no angulation of the abdominal portion of the esophagus was noted. Repeated films yielded similar observations (fig. 10).

Comment.—Experiments on fourteen dogs gave further evidence of the close relationship between the esophagus and the diaphragm. They failed to show that paralysis of one part of the diaphragm seriously impairs the normal function of the esophagus. We did not observe any displacement of the thoracic or abdominal portion of the esophagus following phrenicectomy which was sufficient to offer roentgenologic evidence of obstruction. In dogs we have observed that the lower part of the thoracic portion of the esophagus may be pulled to the side of the normally contracting leaf of the diaphragm. This is in accordance with the observation made by Truesdale.[24] This deflection occurs during inspiration, but the esophagus returns toward the midline during expiration.

We did not make a fluoroscopic examination of our dogs to determine the effect of phrenicectomy on the milking action of the dia-

24. Truesdale, P. E.: Congenital Hernia and Rupture of the Diaphragm, Ann. Surg. **90**:654 (Oct.) 1929.

phragm. Our films nevertheless showed that the abdominal part of the esophagus is filled with barium during expiration and fails to fill during inspiration. A thin barium mixture may outline this part of the esophagus during either phase of respiration.

Whenever left-sided phrenicectomy was followed by a marked rise of the left side of the diaphragm we noted increased angulation of the abdominal portion of the esophagus. This increased angulation, however, was never sufficient to produce evidence of obstruction or delay to the flow of barium from the esophagus to the stomach. Increased angulation was not noted in any case of right-sided phrenicectomy.

Two dogs seemed to show dilatation of the esophagus following phrenicectomy. One of these dogs is still alive, and plates of the thoracic portion of its esophagus show an even dilatation throughout its entire length without any evidence of obstruction at the lower part. We have noted that overfilling with a very thick mixture will result in such an apparent dilatation. We feel confident that this is not the only factor producing dilatation of the esophagus in this animal. It is interesting to note that the dog has become extremely emaciated. He was operated on on Nov. 2, 1929, six months before the present writing. We therefore reserve judgment as to the possible late consequences of phrenicectomy in these dogs.

The following are the answers to the questions that prompted our experimental investigation:

1. There is no evidence at present that phrenicectomy results in obstruction at the lower end of a dog's esophagus.

2. Marked elevation of the left side of the diaphragm may result in increased angulation of the abdominal portion of the esophagus.

3. After unilateral phrenicectomy there is deflection of the lower thoracic part of the esophagus by the normally contracting leaf of the diaphragm.

4. Evidence of slight dilatation of the esophagus has been noted several months after left-sided phrenicectomy.

5. There is no evidence that phrenicectomy can produce cardiospasm in dogs.

THE SO-CALLED GASTROCARDIAC COMPLEX

We noted cardiac symptoms on two occasions following phrenicectomy. These symptoms were palpitation and dyspnea. For this reason we had electrocardiograms made both before and after phrenicectomy. Before reporting our experiences we shall present some general considerations.

Mittenleiter,[25] among others, drew attention to the action of the diaphragm on the circulation. This action may be indirect through

25. Mittenleiter, M.: Die Bedeutung des Zwerchfells für den Blutkreislauf, Deutsche Ztschr. f. Chir. **188**:379, 1924.

changes in respiration, the result of altered intrathoracic or abdominal pressure, or direct through action on the heart and blood vessels.

The greater portion of the inferior vena cava is intra-abdominal. Mittenleiter [25] noted that where it pierces the tendinous portion of the diaphragm there are practically no muscle fibers in the inferior vena cava. As it passes through the diaphragm it becomes rich in elastic tissue and smooth muscle. Anatomically under normal conditions the inferior vena cava should not be compressed, as it pierces the tendinous portion of the diaphragm.

It is conceivable that a diaphragm with an elevated right side might compress the inferior vena cava if adhesions are present. The heart can actually be greatly displaced, rotated or pressed on by an "intrathoracic" liver or stomach, as these organs may become intrathoracic structures following phrenicectomy.

It is appreciated that phrenicectomy may actually do good and may improve the circulation when there are adhesions between the pericardium and the diaphragm (Brauer and Fischer [26]).

It has been observed that the intra-abdominal pressure is greater with abdominal respiration than with thoracic respiration. Mittenleiter [25] expressed the belief that the rise in the diaphragm and the action of the diaphragm alone affect the intra-abdominal pressure but little. He is of the opinion, however, that unilateral phrenicectomy diminishes the sucking action exerted on the veins.

As we are to refer to the term "gastro-cardiac complex" (gastrokardiale Komplex), it is perhaps best to state what this term implies. When Roemheld [27] described this symptom-complex, he spoke of it as a neurosis. Patients so affected apparently have a neuropathic constitution and a heart that readily responds to stimuli. To this nervous basis is added a dyspeptic diathesis because of an accumulation of gas in the stomach. The symptom-complex thus calls for the following underlying conditions: a heart that readily responds to stimuli and is mobile (cor mobile) and a chronic air bubble in the stomach.

PHRENICECTOMY AS A CAUSE OF THE GASTROCARDIAC COMPLEX

In discussing phrenicectomy as a cause of the so-called "gastrokardiale Komplex," Hecht [13] pointed out that the dextrocardia that may result need not per se cause dyspnea. He reported, however, the occurrence of palpitation and extrasystoles in two instances. These

26. Brauer, L., and Fischer, H.: Die Herzchirurgie unter Berücksichtigung physiologischen Fragestellungen, Hand. d. norm. u. path. Physiol. **7**:1877, 1927.

27. Roemheld, L.: Der gastrokardiale Symptomkomplex eine besondere Form sogennanter Herzneurose, Ztschr. f. phys. u. diätet. Therap. **16**:339, 1912.

extrasystoles could have been due to the dyspnea of exertion. Hecht [13] stated further that as long as the musculature of the heart is unimpaired and the circulation intact, phrenicectomy with resultant displacement of the heart should not produce any symptoms. Roemheld [27] would have us believe that a heart already displaced or rotated can be appreciably affected by a diaphragm elevated by an accumulation of gas in the stomach or by loops of distended colon beneath it.

Welles [15] noted that in a small number of his patients there developed a persistent tachycardia and a rise in pulse rate from 10 to 20 beats per minute following phrenicectomy.

Bernuth [28] reported the occurrence of a gastrocardiac complex following left-sided phrenicectomy for bronchiectasis in a girl, aged 12. The operation was performed in June, 1927. The diaphragm rose 2 cm. In November the child complained of palpitation and was cyanotic. The pulse rate was 180 per minute. There were extrasystoles. The electrocardiagram was indefinite. The patient's symptoms were relieved when she was placed on frequent small meals.

Berg [29] pointed out that the gastrocardiac complex can be associated with organic disease, such as gastric ulcer and cholelithiasis.

THE ELECTROCARDIOGRAM AFTER PHRENICECTOMY

We sought to determine from the electrocardiogram whether a rise in the diaphragm following phrenicectomy produces a recognizable change in it. Ten patients had electrocardiograms made before and after phrenicectomy. Nine had electrocardiograms made only after phrenicectomy. In no instance was the presence of organic heart disease demonstrated before phrenicectomy. We are therefore unable to say what effect phrenicectomy would have on an already diseased heart. As already noted, only two patients complained of palpitation and dyspnea. In one instance in which paroxysmal tachycardia was clinically suggested after phrenicectomy the electrocardiogram was normal.

Dr. Julius Jensen of the department of cardiology carefully studied the records of those patients who had the electrocardiogram made before and after phrenicectomy. His report reads:

> The records showed no marked changes. Four records showed no changes whatever and two records showed changes which were not conclusive. In one of these there was inversion of the T waves in lead III. Four showed definite changes in the heights of the complexes but not in their shape.

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28. Bernuth, F. V.: Gastrokardialen Symptomkomplex nach Phrenicusexerese bei einem zwölfjährigen Kinde, Beitr. z. Klin. d. Tuberk. **71**:256, 1922.

29. Berg, H. H.: Zur Klinik der Gastrokardialen Beschwerde, Ztschr. f. klin. Med. **108**:186, 1928.

The following cases illustrate some of the changes noted:

CASE 2.—A girl, aged 18, had abscess of the lung. The mediastinum was not fixed. Right-sided phrenicectomy resulted in a slight rise in the diaphragm. Dr. Jensen reported the following changes: "A left axis deviation with upright T waves in lead III changed to a normal electrocardiogram with inverted T waves in lead III. This effected a lowering of T waves in lead II."

CASE 3.—A woman, aged 20, had bilateral bronchiectasis and a fixed mediastinum. The diaphragm became slightly elevated following a right-sided phrenicectomy. An electrocardiogram showed that the complexes in lead III were heightened and that the T waves of the same lead were lowered after phenicectomy.

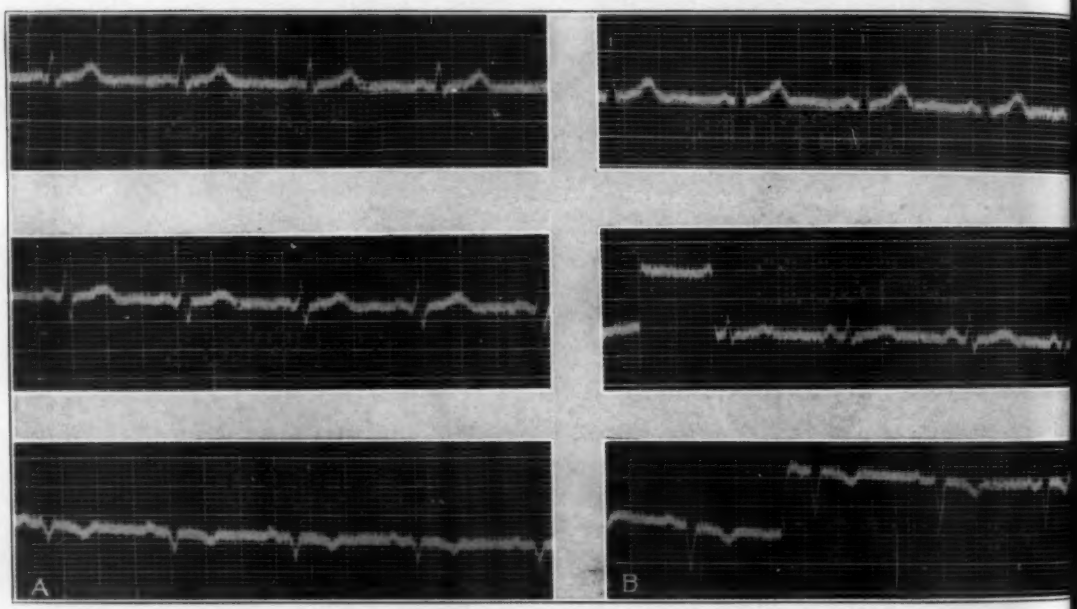

Fig. 11.—Electrocardiograms taken before (*a*) and after (*b*) phrenicectomy in case 3.

CASE 4.—A man, aged 38, had had chronic abscess of the lung and bronchiectasis on the left side. This patient had been treated previously by Dr. Graham by cautery pneumectomy, following which he was well except for an anatomic defect and bronchial fistula. Phrenicectomy was performed as a preliminary step in closing the bronchial fistula. Left-sided phrenicectomy resulted in a high diaphragm and displacement of the heart with apparent rotation of it. The cardiophrenic angle became more acute as a result of displacement of the apex upward. The electrocardiogram showed that the QRS complexes in lead I became higher, and those in lead III deeper, following phrenicectomy (fig. 11).

This patient was later subjected to a complete thoracoplasty and a successful plastic operation following phrenicectomy. Cardiac symptoms did not develop after these operations.

CASE 5.—A man, aged 25, had pulmonary tuberculosis and cavitation on the left side. This patient received pneumothorax treatment before and after phrenicec-

tomy. We believe that elevation of the diaphragm following phrenicectomy was somewhat inhibited by the presence of a large pneumothorax pocket. The mediastinum was not fixed, and there was displacement of the heart into the right side of the thorax. This displacement probably occurred as a result of the phrenicectomy, since the amount of air introduced at refills was the same before and after operation. The electrocardiogram showed that the low or almost inverted QRS complexes in lead III became definitely upright.

Electrocardiograms of nine patients of whose heart action only tracings were made after the operation were considered normal.

The slight changes in the complexes were interpreted as being due to changes in the cardiac axis caused by the altered position of the heart.

SUMMARY

Phrenicectomy may be followed by gastro-intestinal symptoms. Twenty-seven patients were examined before and after phrenicectomy. These patients were given a barium meal and underwent fluoroscopic examination; in many instances roentgenograms were taken before and after phrenicectomy. The phrenicectomies were performed for pulmonary disease. Five patients complained of the following symptoms after phrenicectomy: one of eructations of gas, another of heart burn, a third of vomiting and two of dysphagia. In all but one instance these complaints were temporary. With but one exception, they followed left-sided phrenicectomy. A case of cardiospasm which apparently followed phrenicectomy is recorded.

No marked mechanical displacement or shift of the upper third of the intrathoracic portion of the esophagus was noted after phrenicectomy. Slight respiratory deflection of the lowermost intrathoracic portion of the esophagus was noted. The normally contracting leaf of the diaphragm appears to displace the lower part of the esophagus to its side during inspiration, but permits the esophagus to return to its former position during expiration.

The curve that the esophagus normally makes after it leaves the pillars of the diaphragm to enter the stomach can become sharper following left-sided phrenicectomy. In no case observed was this of serious moment. It is suggested (Moore) that the upward displacement of the stomach might be due to rotation of the greater curvature. Cases that have resulted in only slight elevation of the left leaf of the diaphragm have failed to show any marked change in the position of the abdominal portion of the esophagus. Patients with a large left pneumothorax before and after phrenicectomy showed only moderate elevation of the diaphragm after phrenicectomy and little or no increased angulation of the abdominal portion of the esophagus. We failed to observe permanent change in this part of the esophagus fol-

lowing phrenicectomy. We did observe respiratory deflection of the stomach after right-sided phrenicectomy.

The normal milking action could still be observed following phrenicectomy. We have no absolute proof that phrenicectomy per se may cause obstruction at the lower end of the esophagus.

Experimental studies on dogs yielded data similar to the clinical observations, but gave no evidence of esophageal obstruction following phrenicectomy.

The electrocardiagram showed no marked changes following phrenicectomy. Four patients showed changes in the height of the complexes but not in their shape. Two followed left-sided, and two followed right-sided phrenicectomy.

CONCLUSIONS

1. Gastro-intestinal symptoms of a transient character are not infrequent following unilateral phrenicectomy. They are of no serious consequence.

2. Deflections of the lower thoracic part of the esophagus occur following unilateral phrenicectomy and result from inspiratory contraction of the innervated leaf.

3. Permanent large stomach bubbles and increased angulation of the abdominal portion of the esophagus may occur following marked elevation of the paralyzed left leaf of the diaphragm.

4. The normal milking action of the diaphragm on the esophagus is not impaired by unilateral phrenicectomy.

5. There is no experimental evidence that phrenicectomy results in obstruction of the lower part of the esophagus or proof that phrenicectomy may produce "cardiospasm."

6. The electrocardiograms following phrenicectomy show no marked change.

ABSTRACT OF DISCUSSION

DR. F. T. LORD, Boston: As I remember the cases of eventration of the diaphragm reported in the literature, there are symptoms of circulatory or gastro-intestinal disturbance in about one half of them. This anomaly, when discovered, may be assumed to have been of long duration, and it is a question whether these observations on rather recent cases of phrenicectomy can be regarded as an assurance that symptoms will not later develop. How long after the operation were these cases observed?

DR. HARRY C. BALLON, St. Louis: Some of these patients were observed as long as three and one-half years after phrenicectomy. We do not know at the present time what the late consequences of phrenicectomy will be. It is well known that patients suffering from eventration of the diaphragm go for many years before any sign or symptoms develop. It is therefore possible that in some patients on whom phrenicectomy has been performed, other hitherto unmentioned late consequences may develop after ten or twenty days.

IDIOPATHIC DILATATION OF THE ESOPHAGUS

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MONTREAL, CANADA

The disease variously known as idiopathic dilatation of the esophagus, cardiospasm or achalasia cardia has not rarely been diagnosed since the advent of the x-rays and the opaque meal; by those interested it is generally held to be second only to cancer in frequency of diseases of the esophagus.

The main interest in the study of a disease depends on new evidence of its causation, if that has been in doubt, or new methods of treatment, if those used in the past have been unsatisfactory.

Of the many names offered, the one chosen, "idiopathic dilatation of the esophagus," suggests a confession of ignorance as to the cause, and a brief review of the methods of treatment shows wide divergence in principle.

Recent work by a group in Japan seems to offer a more definite and satisfactory explanation of the pathologic process. I hope to indicate a method of surgical treatment which, if not entirely new, has been only half-heartedly stated and not correlated to the pathologic process, yet which I believe is based on a true understanding of the mechanics of the disease, and which, easy and safe of accomplishment, has been successful in one instance.

It is probable that there has been included within this group more than one series of pathologic changes. These must be distinguished and separately classified. By this, I mean that true cardiospasm may be an entity, but a different disease than idiopathic dilatation.

I have recently had the opportunity to see in a new-born infant a condition that may well be looked on as cardiospasm comparable to infantile pyloric stenosis. Because the infant was vomiting, roentgen examination was made. The fluoroscopic examination showed the esophagus to be a little wider than was expected. The fluid food hesitated at the level of the diaphragm for some moments; there was then a series of strong peristaltic movements in the esophagus; the cardia opened, and the food entered the cardiac end of the stomach. It was immediately and forcibly regurgitated. This was obviously something different from idiopathic dilatation.

Idiopathic dilatation signifies a diffuse enlargement of the lumen of the esophagus in which no mechanical obstruction exists. The dilatation is mostly in the lower two-thirds, that is to say, in the thoracic portion of the organ. The abdominal portion, the portion from 1½ to 2 inches (3.7 to 5 cm.) below the diaphragm, is not dilated.

The esophagus is not only dilated, but also elongated. It may measure up to 46 cm. It must therefore become curved, so that frequently a large fold rests on the upper surface of the diaphragm. Often it may contain from 1,500 to 2,000 cc. of fluid. The wall becomes thickened, the thickening being represented mostly in increase of the circular muscle fibers. The diameter may measure from 6 to 7 cm. to 16 cm. and the circumference 30 cm.

The mucosa may be normal, but more frequently it is inflamed. The tissue is then friable from inflammatory exudates.

The subdiaphragmatic portion requires special mention. It is never dilated. It is often described as normal, and the phrase keeps repeating itself, "thickened and contracted like a lead pencil."

On the three patients on whom I have operated, the subdiaphragmatic esophagus was a small, round, rather firm structure little larger than a pencil. It was not thickened and showed no sign of hypertrophy of the muscle. It measured about 1 cm. in diameter and was round, as compared to the 1 inch (2.5 cm.) diameter and flattened appearance of the normal structure.

Bull, in a publication in 1925, gave details of this portion of the esophagus as found at operation or post mortem in 104 cases. In 52 it was reported normal; in 52 altered. Thirty of these 52 were described as small, contracted, pencil-like or less than 1 cm. in diameter. Only 3 were described as hypertrophied.

It seems clear, therefore, that the cardia is found to be either normal or small, but not thickened.

The only significant microscopic observations are those of Krous and Ridder, who reported finding atrophy of the vagus nerve in one instance, and those of Rakes who found what he believed to be atrophy of Auerbach's plexus in three instances.

Bull reported that in 82 of 141 patients symptoms following the ingestion of food appeared before the age of 40.

The most important observations in a macroscopic study of the pathologic changes in the disease are that the dilatation occurs in the thoracic portion of the organ and ceases abruptly at the level of the diaphragm. Below this point, in the great majority of instances, it is a round cordlike structure which shows no increase in thickness of the muscular wall.

The esophagus is also lengthened, and may be folded over the surface of the diaphragm. The mucosa may be very friable or ulcerated, a point to be seriously considered in any form of manipulation.

Starting from this point, a group of Japanese investigators headed by Tamiya, have published a series of experimental studies which have gone far to explain the occurrence of the disease. From experiments

on the reaction to drugs of isolated strips of esophagus taken from the subdiaphragmatic portion, the details of which it is not necessary to elaborate, Tamiya concluded that the subphrenic part of the esophagus is supplied by both vagus and sympathetic fibers, and that the sympathetic fibers are mostly depressors.

The second step consisted of fluoroscopic studies on the esophagus of dogs after one-sided section of the vagus, the sympathetic and the vago-sympathetic trunk. This resulted in a marked delay in the passage of the food at the lower end of the esophagus. A pendulum movement developed, but the food did not pass on. This cannot be regarded as spasm, because there was never any resistance to the passage of bougies. The delay could also be overcome by filling the esophagus with fluid. A spastic closure does not occur, but there is failure to open, an achalasia. The closure of the cardia is then due to the normal autonomic tone.

The stoppage of food after the one-sided section was never permanent, and did not occur after a variable time, from days to weeks. It was not accompanied by dilatation. The result of the cutting of both vagi was a total loss of peristaltic action, a widening of the lumen and a stoppage of food at the level of the diaphragm.

The widening of the esophagus resembles that found in idiopathic dilatation. The cardia is closed from then till death, but not during a spasm. There is no resistance to the passage of bougies. Resistance can be overcome by filling the esophagus with water, which, when acting directly by its weight, opens the cardia.

An effort was then made to produce the same results by causing a degeneration of the nerves by painting with arsenic. Immediately after the treatment by arsenic, the food passed normally, but within twenty-four hours, concurrently with the appearance of sympathetic paralysis in the eye (myosis, ptosis and bulbar retraction), there was interference with the passage of food more or less similar to that occurring after cutting, and depending on the degree of degeneration of the vagi.

These experiments give strong support to the theory of Krous' that the disease is secondary to degenerative changes in the vagi, and that the closure is due to the normal tone acting without nerve control. The clinical picture is fairly constant. For the diagnosis, two things are of great importance, the history of the onset and progress of the disease and roentgen examination.

The history of the condition usually begins before the patient is 40 years of age, and extends over years. There is mainly difficulty in swallowing food. Sometimes the onset is sudden, but progress is intermittent. As the disease progresses, regurgitation of large quantities of food becomes a feature. This food is frothy and mixed with saliva. The regurgitation of large quantities of food is in marked contrast to

the dysphagia of mechanical obstruction, for in the latter the esophagus never contains the 1,500 to 2,000 cc. common in idiopathic dilatation.

The patient nearly always has learned certain tricks or contortions to aid the passage of food, and these have two common purposes: to straighten out the elongated and crumpled esophagus and to add weight to the column of fluid. Thus these patients may stand up, raise the chin and stretch the neck like a chicken drinking, and following the ingestion of food they may drink glass after glass of water. Some have been reported to be able to judge when the food has passed and then reject the water.

There is no more than the normal resistance to the passage of a bougie or stomach tube, and most persons have been fed by this means at times or constantly.

The long effort, the regurgitation and the contortions are most distressing to the patients, and usually to those who have to eat in their presence.

The roentgen appearance is also characteristic. In no other disease is there seen the wide shadow associated with this condition. The shadow ends at the level of the diaphragm as a smooth, rather bluntly pointed cone without the length of constriction or the irregularities of outline found in carcinoma.

The histories of the three cases here reported are illustrative of the disease.

REPORT OF CASES

CASE 1.—Mrs. D., aged 50, was admitted to the hospital on Nov. 1, 1926, complaining of difficulty in swallowing food. She first noticed this difficulty more than ten years before. After eating, she had pain at the lower end of the sternum. Her discomfort gradually increased, until during the past year she had great difficulty in getting enough food to keep her alive. She had lost about 50 pounds (22.7 Kg.) and weighed 87 pounds (39.5 Kg.). She took from two to three hours to eat a meal, using large quantities of water between mouthfuls. She twisted her head backward and to one side, held her breath and forced the food down. Often this resulted in regurgitation of most of the food taken. She ate alone. At times she was fed by tube. Dilatation by bougies and dilatation of the bag was tried, with only temporary relief. She urged that something be done.

Roentgen examination showed marked dilatation of the esophagus. Semisolid food remained in this organ, but fluid passed into the stomach, leaving a column about 3 inches (7.6 cm.) high in the lower end of the esophagus. The shadow ended bluntly at the level of the diaphragm.

Extramucosal esophagoplasty was performed on Nov. 15, 1926, Marwedel's incision being used. The subdiaphragmatic portion of the esophagus was less than half an inch (1.27 cm.) in diameter. The muscle wall was not thickened, but felt like a muscular cord. Immediately above the diaphragm, the esophagus was 1½ inches (3.7 cm.) in diameter. The dilated portion was brought through the diaphragm, and the muscle incised down to the submucosa well on to the

cardiac end of the stomach. The wound was closed without drainage. From the time of operation to the present day, she has taken food freely. She gained 30 pounds (13.6 Kg.) in weight, eats her meals with the rest of the family, and is living a normal life.

Roentgen examination somewhat over a year after operation showed that the esophagus filled with food 6 inches (15.2 cm.) above the diaphragm before any passed into the stomach; then the whole mass passed on rapidly.

CASE 2.—J. P., aged 35, was admitted to the hospital on Feb. 27, 1928. The condition began about nine months before admission, the onset being characterized by sudden acute pain and regurgitation of food. The regurgitated material contained undigested food, water and saliva. The food was returned about five minutes after ingestion, following a sensation of the food sticking at the lower end of the sternum. The patient's appetite was good, and she complained constantly of hunger. The symptoms became persistent and severe. She lost 49 pounds (22.2 Kg.) and felt dizzy and weak from lack of food.

Atropine was tried without benefit. Feeding by tube was instituted. The tube passed easily. Roentgen examination showed a six hour retention of food at the cardiac end of the esophagus, a column of barium 6 inches long and an empty stomach.

On February 28, a Heller extramural esophagoplasty was attempted on the strength of the success in the previous case. The subdiaphragmatic portion of the esophagus was found to be three-fourth inch (1.9 cm.) in diameter. The wall was thin. The muscular wall over the cardiac end of the stomach was incised down to the submucosa, and the cut was extended up onto the esophagus. The procedure seemed satisfactory up to this point, when, without obvious reason, a small leak was observed. This quickly enlarged to a hole one-fourth inch (0.63 cm.) in diameter as if the mucosa was either ulcerated or very soft. The opening was sutured and reenforced by peritoneum; a pad of omentum was sewn over this, and the wound was closed with a drain to the line of suture.

The patient died on the sixth day from an obvious mediastinal infection.

Autopsy showed a longitudinal opening in the esophagus 6 cm. above the sutured incision. Microscopic section showed a thin necrotic margin. There was no change in Auerbach's plexus similar to that described by Rakes in *Guy's Hospital Reports* of 1920.

There have been advocated a variety of methods of treatment. It is not my intention to discuss these in detail. It is natural that the simpler methods should be tried first, and that operation should not be urged in the less severe cases; but, according to my understanding of the disease, these will be found ineffective and not without danger in the more severe types of the condition.

The methods of treatment have followed in general two main plans: The first methods include dilatation of the narrowed portion of the esophagus either from the inside by bougies or by dilatable bags or dilatation by the finger introduced through an opening through the stomach.

If the pathologic process as described by Tamiya is correct, neither of these methods can be considered either sound in principle or without

the danger of tearing the narrow, relatively thin-walled, friable subdiaphragmatic portion of the esophagus.

The second main line of treatment followed was the formation of an opening by suture between the dilated portion of the esophagus and the stomach. The objection to this is its danger, for though it has been successfully done a number of times, suture of the esophagus is notably unsatisfactory. Especially is this true in the inflamed state, when the tissues are sometimes so friable as to make suture most precarious.

The third method is that adopted successfully in the first of the three patients whose cases are reported here. Encouraged by the success in the first case, I attempted the same method in the second case, only to find tissue so friable or ulcerated that the mucosa was either absent or torn into the lumen; the sutures sloughed out, resulting in a fatal infection of the mediastinum.

In the third case, the various surgical procedures were reviewed.

The first consideration was that in the most commonly adopted surgical methods one step was common to all. At one stage of the operation, the opening through the diaphragm was enlarged and the dilated portion of the esophagus brought down through the opening and held there by sutures.

The second consideration was suggested by the fluoroscopic examination of the first patient after the extramural esophagoplasty. Here the first view suggested that nothing had been accomplished, but when the column of fluid in the esophagus had reached a height of about 6 inches the resistance of the narrow subdiaphragmatic portion was overcome, just as it was overcome in Tamiya's experiments, and the food passed freely into the stomach. This was in marked contrast to the appearance before the operation, when the whole esophagus could be filled and remain full for long periods or until regurgitated. What was the difference? It seemed reasonable to suppose that when the dilated portion ended at the diaphragm, over-filling of the esophagus merely resulted in a still more marked kink just above the diaphragm, while after the opening of the diaphragm was enlarged and a part of the dilated portion brought through, the weight of the column of fluid could then act to a mechanical advantage and overcome the normal tonic resistance of the narrowed portion of the esophagus leading into the cardia.

In retrospect, it seemed unlikely that the extramucosal esophagoplasty in the absence of any thickening or hypertrophy of the muscles could be considered comparable to the Fredet-Ramsted pyloroplasty so successful in infantile pyloric stenosis. Moreover, the tissue conditions found in the second case, with the consequent wounding of the mucosa

and the sloughing of the infected wall, had demonstrated that extramucosal esophagoplasty was dangerous besides being unnecessary.

In the third patient, it was therefore deliberately planned that the operation should consist merely in the earlier steps, i. e., the exposure of the cardiac end of the stomach through the Marwedel incision, the cutting of the coronary ligament of the liver and the turning downward and to the right of the left lobe of the liver. By this means the cardiac end of the stomach and the subdiaphragmatic portion of the esophagus are brought into view. Under the eye an incision was then to be made forward through the crura of the diaphragm. The dilated portion of the esophagus was brought through this opening for an inch or more. The main opposition is found in the vagi, which may be cut with impunity, more especially if Tamiya is correct in stating that they are already degenerated.

Case 3.—Mrs. B. M., aged 58, was admitted to the hospital on May 20, 1929. She had previously been admitted to the otolaryngologic department under Dr. Birkett in 1926. At that time she complained of difficulty in swallowing of one year's duration. The difficulty was more apparent with solid food than with fluid. She then had the sensation of "filling up" inside. If she tried to swallow after this she had to force the food down by violent efforts, often regurgitating through the nose. After a short rest, she forced another mouthful of food down.

In October, 1926, she was examined with the aid of the esophagoscope, and the cardiac end of the stomach was found markedly contracted and compressed about a large bougie, which could be easily passed. Roentgen examination demonstrated obstruction of the characteristic kind at the end of the diaphragm.

The patient was admitted to the surgical wards three years later in May, 1929.

The subsequent history showed gradually increasing difficulty in swallowing with frequent regurgitation of food. During the winter of 1928-1929, she had to be fed by tube during an acute illness. Since that time she had learned to pass the tube herself, and all nourishment was taken by this means. She lost 80 pounds (36.3 Kg.) during the three years.

On May 29, 1929, she was operated on, the same approach being used as in the other case, and the subdiaphragmatic portion of the esophagus was exposed. The opening between the crura of the diaphragm was enlarged by cutting forward until it admitted two fingers easily. The esophagus was then freed by blunt dissection and pulled down till 1½ inches of the dilated portion was brought through. To allow of this, the vagi were cut. The subdiaphragmatic portion of the esophagus was a small, round, cordlike structure about 1½ inches long and not more than ⅓ inch (0.7 cm.) in diameter. There was no hypertrophy of the circular muscle coat. Immediately above the diaphragm, the esophagus was 1½ inches in diameter, but not notably hypertrophied. The wound was closed without drainage.

The patient's recovery was smooth, and she has been able to swallow soft and liquid food in ordinary time. She sometimes has a sensation of fulness for from ten to fifteen minutes, which might suggest that food remained a time in the lower end of the esophagus. She has gained weight and strength.

By the operative procedure used here the grave danger of tearing the esophagus is avoided, as the dangerous suture is not necessary.

Since the peristaltic movements of the esophagus are no longer operative in any case, the onward passage of food must depend on the pressure exerted by the column of fluid in the esophagus. The recognition of this mechanical factor seems to be essential to success in any operation. This procedure recognizes this factor; further, it is simple to carry out and should be free from the accident that is constantly to be feared in every other mechanical treatment—the tearing of the friable, inflamed esophagus.

On theoretical grounds, there should be no tendency to recurrence, for any cicatrix at the opening of the diaphragm would tend to widen, not to contract, the new opening.

The success attending the operation on the last patient is encouraging. Food can now be taken in good quantity and in ordinary time; the only precaution is that the food must be well divided and mixed with a fair quantity of fluid.

ABSTRACT OF DISCUSSION

DR. A. T. BAZIN, Montreal, Canada: As Dr. Scrimger says, it is unfortunate that we cannot decide on the terminology. To my mind, "idiopathic dilatation" is an unsatisfactory term to describe this condition, unless there are a few cases that are associated with no causative lesion whatsoever. Many terms have been given to this disease, or subdivision of this disease if there are such, e. g., achalasia, an inability to relax. I do not see why we cannot be satisfied with "cardiospasm," provided we understand the anatomy and appreciate that it is not spasm of an orifice that we are dealing with, but spasm of a sphincter, and that the cardiac sphincter of the esophagus is at the level of the diaphragm. Moreover, it is easily pushed up above the level of the diaphragm.

I have had a limited experience with this malady. In fact, it seems to be difficult to educate the internists in the idea that cardiospasm is not purely a neurosis; they therefore hold these cases for an indefinite length of time. I have had three cases in the past two years; one of these, observed recently, was in a man, 23 years of age.

There is a very decided neurotic taint in all these cases. One of my cases occurred in a farmer's wife who stated that she was overworked and was anxious to have her husband move off the farm. The second patient was a country clergyman's wife. She ought to have been dissatisfied, but she did not say that she was. The third patient, already mentioned, a farmer's son who had been trying to get away from the farm for several years. He showed evidences of flushing on the slightest provocation and sweating of the palms of the hands. Two of the patients are well and one is dead.

I have been impressed especially by the description of the disease by Abel, in his monograph published a few months ago, and by the treatment advised by A. J. Walton, of London, that is, manual divulsion through the stomach.

In the fatal case the patient died of an abscess of the lung with secondary empyema. She had a huge dilated esophagus. It is well known that a common mode of death in these atonic cases, in which there is great dilatation and accumulation of putrefied food, is inspiration from overflow during sleep. I cannot prove it, but I am inclined to think that the infection developed in the lung prior to operative intervention.

I believe that it is a bad plan to perform an operation in these cases until by gastrostomy one has restored the emaciated, dehydrated and nonresistant patient to the semblance of health.

DR. F. A. C. SCRIMGER, Montreal, Canada: I neglected the cardiospasm, because I still do not believe any spasm was present. I should like simply to reemphasize what I believe to be the real danger. In divulsion when you can have the material right on your hand and can see what you are doing, you can perhaps realize the dangers better than if the hand is introduced into the incision and the operation is done out of sight. In the fatal case that I had it appeared to me that the patient could not have stood any kind of dilatation.

HYDATID CYSTS OF THE LUNG

REVIEW OF THE RECORDED NORTH AMERICAN CASES *

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It is my purpose in this paper to call attention to the possibility of hydatid disease originating in American born persons and to collect the cases of the cysts of the lung due to infestation with *Taenia echinococcus* that have been reported in North America. In an address before the Clinical Congress of the American College of Surgeons at Montreal in 1926, Barnett [1] made the statement that hydatid disease is increasing so rapidly in some of the South American countries as to constitute a national peril. In 1922, N. H. Fairley [2] said that there had been no reduction during the preceding ten years in the number of cases admitted to the Melbourne hospitals. Many references can be found in the literature from the countries where infection with *Taenia echinococcus* is common showing an increased prevalence of the disease among the domesticated animals. Most of the known facts about this disease have come from the experience of such men as Deve, Dew, Bird, Fairley, Barnett, Finochietto, Morquio, Escudero, Vegas, Cranwell, McKay and many others working in localities where the infestation is common. In spite of the vast amount of work being done in these regions represented by portions of France, Australia, New Zealand, Iceland, Italy, the Argentine and other South American countries, Spain and Germany, the disease has not been eradicated. This parasite exists in North America, and from time to time cases of hydatid disease have been reported in the natives of the United States and Canada. Of the 241 cases collected by Lyon,[3] 9 per cent occurred in persons born in America. In 68 cases that Magath [4] gathered from the literature between Lyon's report in 1901 and 1921, the incidence in native born persons was 5.9 per cent. In the group of 36 cases of hydatid cysts of the lung reported in this paper 2 occurred in persons known to have

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1. Barnett, L. E.: Recent Advances in Knowledge of Hydatid Disease, Surg. Gynec. Obst. **45**:148, 1927.

2. Fairley, N. H.: The Complement Fixation Test for Hydatid Disease and Its Clinical Value, M. J. Australia **1**:341, 1922.

3. Lyon, I. P.: A Review of Echinococcus Disease in North America, Am. J. M. Sc. **123**:124, 1902.

4. Magath, T. B.: Echinococcus Disease: Etiology and Laboratory Aids to Diagnosis, M. Clin. North America **5**:549, 1921.

been born in the United States. Scattered reports of infestation among domesticated animals have appeared, but there has been, as far as I can determine, no concerted action to treat the situation with the thoroughness that its seriousness demands. The history of echinococcus disease in countries much more alive to its dangers than the United States shows no reason to expect natural diminution. Is there not reason to fear that this country is on the threshold of a period in which there will be a serious increase of hydatid disease among the native born population? There is surprisingly little information available as to the incidence of the infestation of animals in this country and Canada. *Taenia echinococci* have rarely been found in dogs in this country. In Washington, D. C., Curtice [5] recovered the parasite from a dog about forty years ago, and several years ago Kaup [5] in Kansas reported that it was found in dogs. Occasional reports of a search with negative results have been recorded. From 1877 to 1882, Osler [6] failed to find *Taenia echinococcus* in several scores of dogs examined in Canada. Swine are more commonly infested in North America than the other domesticated animals. In 1882, Osler and Clement,[7] in a study of the parasites in the pork supply of Montreal, were able to demonstrate infestation in 1 of every 33.4 examined. Lyon, in 1902, quoted Stiles, then zoologist of the Bureau of Animal Industry, Washington, D.C., to the effect that there was an undoubted increase in the incidence of infestation among domesticated animals. Johnston and Willis [8] reported several epidemics occurring in hogs in Virginia during 1913 to 1914. In one consignment of 46 hogs, from Charles City County which were slaughtered in Richmond, there was 100 per cent infestation. In another shipment of swine from Goochland County, 5 of 8 had hydatid cysts. In November, 1917, they reported 25 per cent of infestation in a shipment of 60 hogs from Charlotte County. These authors quoted Hall as saying "recent abattoir figures show an alarming increased prevalence of the disease in domestic animals in some parts of this country, notably in certain localities in Virginia, Arkansas and Oklahoma." Radcliffe,[9] in 1921, reported hydatid cysts in 100 per cent of a herd of 87 hogs. In a personal communication from Maurice C. Hall,[10]

5. Cited by Hall: Personal communication to the author.

6. Osler, William: Echinococcus Disease in America, Am. J. M. Sc. **84**:475, 1882.

7. Osler, William, and Clement, A. W.: An Investigation Into the Parasites in the Pork Supply of Montreal, Canad. M. & S. J. **11**:334, 1882-1883.

8. Johnston, G. B., and Willis, M.: Hydatid Cyst of the Liver with Report of Two Cases, Surg. Gynec. Obst. **25**:101, 1917.

9. Radcliffe, A. A.: Infestation of a Herd of Swine by Hydatids, M. Rec. **99**:146, 1921.

10. Hall, Maurice C.: Personal communication to the author.

chief of the Zoological Division, Bureau of Animal Industry, Washington, D. C., it was stated that figures regarding the incidence of hydatids in domesticated animals in this country are not available. "In general, it may be said that hydatids are not generally distributed throughout the United States and that they have a patchy distribution, not well known. They are said to be prevalent in parts of New Mexico, Oklahoma and Arkansas; we can always obtain them on rather short notice from our inspection service at Richmond, Virginia; they are found from time to time at various abattoires. In 1927, Morris reported that they occurred in 5 per cent of swine at Baton Rouge, Louisiana, and that the former incidence was 20 per cent. Dr. Jalen, our inspector at Cincinnati, Ohio, reported in 1927 that less than 1 per cent of swine at that station were affected." An attempt to ascertain the incidence of hydatid infestation in this portion of the country followed the discovery that one of the patients whose case is reported in this paper was born and has always lived in this locality. A personal communication from P. Olafson,[11] pathologist, New York State Veterinary College at Cornell University, stated that he has failed to find the parasite during the past three or four years in the routine autopsy on approximately 1,000 of all species of the common domestic animals. He further stated, however, that in pathologic specimens sent from the packing plants in Buffalo, the echinococcus cysts are occasionally included.

Osler, in 1882, made the first collection of hydatid cysts in man in North America. He was able to find 61 cases from recorded case reports, museum collections and personal communications. This group included 5 pulmonary hydatid cysts. Sommer,[12] in 1895, brought the list of recorded cases of echinococcosis up to 110. Up to July 1, 1901, Lyon collected 241 cases of which 4.5 per cent or 11 cases, showed pulmonary cysts. In 1921, Magath added 68 cases from the literature and another 25 cases with hydatid disease that had been observed at the Mayo Clinic in the history of the institution. Five of this group of 93 patients had hydatid cysts of the lungs. Mills,[13] in 1925, made the statement that 18 pulmonary cysts were added to the literature since Lyon's report in 1902, but he did not give a list of the cases.

In a search of the literature, I have been able to collect 34 cases of pulmonary hydatid cysts which, together with the 2 cases recorded in this paper, make the total of 36 known cases. In this report are

11. Olafson, P.: Personal communication to the author.

12. Sommer, H. O.: Echinococcus Disease in the United States, New York M. J. **62**:656, 1895.

13. Mills, H. W.: The Surgical Treatment of Echinococcosis, M. J. & Rec. **122**:407, 1925.

included as cases of cysts of the lung instances that Lyon's paper classified as secondary invasion of the pulmonary tissue from the rupture of adjacent cysts, especially subdiaphragmatic. I have accepted as primary hydatid cysts of the lung all those cases with a fairly definite picture of an intrapulmonary cyst, whether or not there was evidence of multiple infestion of other localities in the body. Incidences of secondary involvement of the lungs, usually expressed by the expectoration of the hydatid elements following the penetration of the diaphragm and adherent lung by a cyst of the liver, are not included. Morton and I,[14] in a study of the literature of bronchobiliary fistula, found that the most common cause of this unusual condition was the rupture of an echinococcus cyst or an amebic abscess of the liver through the diaphragm into an adherent lung and thence into the bronchial tree. Neisser[15] said that 11 per cent of hydatid cysts of the liver break through into the respiratory apparatus. The acceptance of several of the cases herein reported may be questioned both as to the true nature of the pathologic process, because of the absence of the microscopic demonstration of scolices or hooklets, and because of the difficulty in determining the exact intrathoracic location, in several of which the cysts may have been pleural rather than pulmonary. Primary infestation of the pleura is rare. Neisser and Madelung[15] found 1.5 per cent in a collection of 1,179 cases of hydatid disease.

INCIDENCE OF PULMONARY INVOLVEMENT IN HYDATID DISEASE

Next to the liver, the lung is the most common organ to be invaded by *Taenia echinococcus*. Various statistics give the percentage of involvement of the lung up to 20 per cent. Greenway[16] collected 2,740 cases of hydatid cysts over a period of eleven years in which the incidence of pulmonary involvement was 14.69 per cent. In Algiers, Lavillat[17] found cysts of the lungs in 15.7 per cent of 210 cases. He quoted Lemaire who gave the incidence of 2,169 cases as 1:5.4; Prat, 1:3.5, and Finsen, 1:36.5. Vegas and Cranwell[18] reported an 8.5 per cent incidence of cysts of the lung, and Barnett found 10 per cent

14. Morton, J. J., and Phillips, E. W.: Bronchobiliary Fistula, Arch. Surg. **16**:697 (March) 1928.

15. Quoted by Lord, F. T., in Osler: Modern Medicine, Philadelphia, Lea & Febiger, 1927, vol. 4, p. 285.

16. Greenway, D. J., cited in Foreign Letters (Buenos Aires), J. A. M. A. **79**:2019 (Dec. 9) 1922.

17. Lavillat, Francis: Hydatid Cysts of the Lung with a Report of Five Cases, Internat. Clin. **2**:47, 1922.

18. Vegas, M. H., and Cranwell, D. J.: Hydatid Cysts, in Nelson's Loose Leaf Medicine, New York, Thomas Nelson & Sons, 1920, vol. 2, p. 434.

of all cysts in the lung. Dew's [19] figures are also 10 per cent for involvement of the lung.

Multiple infection is common. N. H. Fairley said "echinococcosis more often than not is a multiple infestation." K. D. Fairley,[20] in his study of 33 hydatid cysts of the lung in the Melbourne Hospital, found multiple organs involved in 39.4 per cent. However, in a study of 112 cysts of the lung occurring in children, Morquio [21] stated that the cysts in most cases were primary and isolated. In addition to the frequent involvement of other organs, multiple cysts occur in the lungs. There may be many cysts in both lungs, apparently as the result of a secondary sowing from a primary cyst breaking through into the blood stream. This is strikingly illustrated in Gurlee's [22] case in which the primary cyst occurred in the wall of the right auricle. In the group of North American cases of cysts of the lung collected in this paper, there are only 6 that are conclusively multiple in the lungs. There are 16 cases in which it is impossible to determine definitely, from a study of the records, the exact number of pulmonary cysts, although the probabilities favor a single cyst in the majority of these cases. In 14 instances there seems to be sufficient evidence to judge that a single cyst was present.

EVOLUTION OF A PULMONARY HYDATID CYST

The adult stage of the life cycle of *Taenia echinococcus* is lived in the upper intestinal tract of the dog and doglike animals. This parasite is the smallest of the tapeworms, measuring only from 4 to 6 mm. It possesses 4 segments, the terminal one of which produces large numbers of ova. Barnett said that there are about 500 fertile ova in each ripe proglottis. Innumerable ova are passed out with the excrement. In one way or another these ova gain entrance to the body of the intermediary host. It is most commonly stated that the infestation occurs through contaminated drinking water or vegetables that are eaten raw. According to Barnett, the transmission is usually direct from the dog to the hands and hence to the mouth, in man, and sheep and cattle pick up the infection from contaminated herbage. Deve [23] and Strawell [24] expressed the opinion that infestation occurs during infancy and child-

19. Dew, quoted by McKay, W. J. S.: M. J. Australia **1**:7, 1926.

20. Fairley, K. D.: The Results of an Analysis of Thirty-Three Cases of Hydatid Disease of the Lung, M. J. Australia **1**:341, 1922.

21. Morquio, L.: Echinococcosis of the Lung in Children, Arch. de méd. d. enf. **29**:72, 1926.

22. Gurlee, C. G.: A Case of Echinococcus Disease of the Heart and Lungs, Illinois M. J. **8**:85, 1905.

23. Deve, F.: L'Echinococcose de l'enfant, Arch. de méd. d. enf. **21**:225, 1918.

24. Strawell, R. R.: Symposium on Hydatid Disease, Brit. M. J. **1**:673, 1927.

hood. This is the period when the greatest contact exists between the dog and human beings.

Unlike *Taenia solium* and *Taenia saginata,* the larval stage of *Taenia echinococcus* occurs in the intermediate host. The name, hydatid cyst, has been given to this larval stage as it occurs in man and in from 30 to 40 other mammals, most commonly sheep, swine and cattle. Following ingestion, the embryo is freed from its protective covering by the digestive juices and, passing through the intestinal wall, enters either the blood stream or the lymphatic system. By way of the blood stream, it may reach the lung through the general circulation or through the portal system. The size of the embryo is from 20 to 25 microns (Brumpt), and it can traverse the capillaries by molding itself as do red blood cells (Lavillat). Neisser [25] advanced the theory that the embryo entered the thoracic duct and reached the general circulation at the subclavian vein. Morquio [21] suggested that the ova may reach the lung through the respiratory route. It was formerly thought that the action of the gastric juice was necessary to liberate the ovum from its capsule. However, Deve [25] showed that cysts may be produced by the subcutaneous implantation of ova, and, according to his opinion, the action of the leukocytes is sufficient to liberate the ova from its capsule. The low percentage of pulmonary cysts in Iceland, where Finsen [25] reports 1 cyst of the lung for 36.5 cysts elsewhere in the body, may be taken as favoring this theory as Iceland is said to have a great deal of moisture with little dust. K. D. Fairley stated that the embryo reaches the lung by active migration and that it is improbable that the embryo is conveyed to the lung by the blood stream in any but occasional cases. He based this conclusion from his study of a group of 33 cases, in 27 of which he found the hydatid cyst to occupy the lower portion of the right lung. He also stated that the embryo usually reaches the liver through the blood stream, and then by active migration transports itself to the lung. This theory is not supported by the figures of Heuser [26] who, in a study of 100 pulmonary cysts, found that the left lung was more frequently involved.

The hydatid cyst develops from the embryo, which has lodged in the pulmonary parenchyma. The cyst consists of an outer lamellated, very elastic cuticle and an inner parenchymatous or germinal layer. Pulmonary cysts grow more rapidly than cysts elsewhere in the body because of the lack of resistance to expansion offered by the compressible lung tissue. Escudero [25] stated that two years elapse from the time of infestation until there is sufficient growth to produce clinical symptoms. As the cyst grows, an adventitous layer of fibrous tissue

25. Quoted by Lavillat (footnote 17).

26. Heuser, C.: Hydatid Cyst of the Lung, Am. J. Surg. **4**:486, 1928.

forms from the host surrounding the invader. When the cyst has reached about the size of a walnut, brood capsules arise from the germinal layer producing great numbers of scolices. Dew [27] stated that a univesicular cyst is the typical morphology of hydatid disease, and that daughter cyst formation is a defensive reaction of the mother cyst against trauma, either mechanical, chemical or infective. The cysts of the lung usually do not contain daughter cysts. Dew reported only two with daughter cysts in twenty pulmonary hydatids. In examining hundreds from sheep he found three cysts of the liver and lung with daughter cyst formation. "Whenever an intrathoracic cyst is found to contain daughter cysts, an hepatic origin should be suspected and this should lead to an investigation of the diaphragmatic region" (Dew).

The fate of the enlarging pulmonary hydatid cyst depends on its nourishment, the effect its pressure causes on the surrounding tissues and its location within the lung. According to Dew, the cyst depends on osmosis for nutrition, and consequently possesses a narrow margin of safety. The total lack of any evidence of connection between the endocyst and the adventitous fibrous layer of the host was strikingly illustrated at operation in my first case. Following removal of the fluid contents of the cyst by aspiration and the release of intracystic pressure, the endocyst was found lying free in the cavity formed within the pulmonary tissue. Bird [28] said that although obsolescence may occur, the majority of cysts rupture sooner or later. Erosion into a blood vessel is a common occurrence and occasionally may excite a fatal hemorrhage. Bird reported the cases of two patients who died in this manner. Rupture into a bronchus is the most frequent accident affecting the progress of the cyst's development. Finochietto [29] emphasized the importance of the localization within the lung in reference to the effect of rupture of the cyst into a bronchus. He recognized two groups as determined by their position in the lung, the central and the peripheral. The central cysts develop near the hilus and may be silent for a long time. Pressure gradually causes thinning of the bronchial wall, finally rupture of the cyst takes place into the bronchus. The contents of the cyst are then expectorated, and if the opening into the air passage is sufficiently large, the germinative membrane may pass and recovery follow the retraction and cicatrization of the walls of the cavity. If the opening into the bronchus is too small to permit passage

27. Dew. H. R.: Daughter Cyst Formation in Hydatid Disease: Its Causation and Effects, M. J. Australia **2**:497, 1925.

28. Bird, F. D.: Hydatids of the Lung, M. J. Australia **2**:505, 1925.

29. Finochietto, E.: The Treatment of Hydatids of the Lungs, Practitioner **119**:10, 1927.

of the endocyst, infection occurs in the ruptured cyst and the picture becomes that of a bronchopulmonary suppuration. Bird said that infection within pulmonary cysts always follows rupture in contradistinction to cysts of the liver, which are frequently infected without rupture. The peripheral cysts involve the pleura soon causing pleural pain. Following rupture into a bronchus, according to Finochietto, the cyst near the periphery of the lung never evacuates its contents completely spontaneously, and cure by vomica cannot take place. Occasionally the cyst may rupture into the pleura or pericardium. After infection has occurred in the cyst, rupture into the pleural cavity results in pyothorax or pyopneumothorax. An uncomplicated cyst may rupture into the pleura, producing a hydrothorax, or if rupture into a bronchus is simultaneous, a hydropneumothorax occurs. Living scolices reaching the pleural cavity from the ruptured cyst of the lung may cause grafts to take place on the pleura. This happens rarely in pulmonary cysts. The metamorphosis of scolices into a new generation of cysts used to be termed a biologic heresy, but it is a common occurrence (Barnett). Dew [30] considered it an established fact that daughter cysts, brood capsules and scolices can implant themselves and form new hydatid cysts (fig. 1).

SYMPTOMS

The symptoms of pulmonary hydatid disease vary according to the condition of the cyst. They may be divided into two groups, i. e., those produced by the uncomplicated cysts and those which follow rupture of the cyst. During the early period of the growth of the parasite in the lung, few if any symptoms are produced. Except for occasional anaphylactic phenomena, the echinococcus is well tolerated by the host until because of its size, pressure is made on surrounding structures. Loss of air space by compression of lung tissue results in shortness of breath. This occurs only when the cyst has reached a considerable size, as the normal vital capacity is so greatly in excess of the ordinary air requirement. Pressure on bronchi excites the cough reflex, and cough, slight or severe, is the commonest symptom. Erosion of the walls of blood vessels finally results in ulceration opening into the lumen of a vessel, and hemorrhage into the bronchial tree follows. Hemoptysis is an important symptom in pulmonary infestation. Lavillat said that pulmonary cysts that have never given rise to hemoptysis may be considered as rare. In a series of thirty-eight pulmonary cysts, Jaureguy [31] found hemoptysis in 100 per cent. Pain, probably arising from pleural

30. Dew, H. R.: The Mechanism of Daughter Cyst Formation in Hydatid Disease, M. J. Australia **1**:451, 1926.

31. Jaureguy, M. A.: Hemoptysis Due to Hydatid Disease, An. de Fac. de med., Montevideo **12**:681, 1927.

irritation, may be mild or very severe. K. D. Fairley, in a study of thirty-three cysts of the lung, found cough in 100 per cent, hemoptysis in 57.6 per cent, pain in 54.4 per cent and dyspnea in 27.3 per cent of cases.

At the time of rupture there is a flooding of the bronchial tree with salt water, even to the extent of drowning. When a communication has been established between the cyst and the respiratory tract, the cough becomes more productive, and pieces of the wall of the cyst may

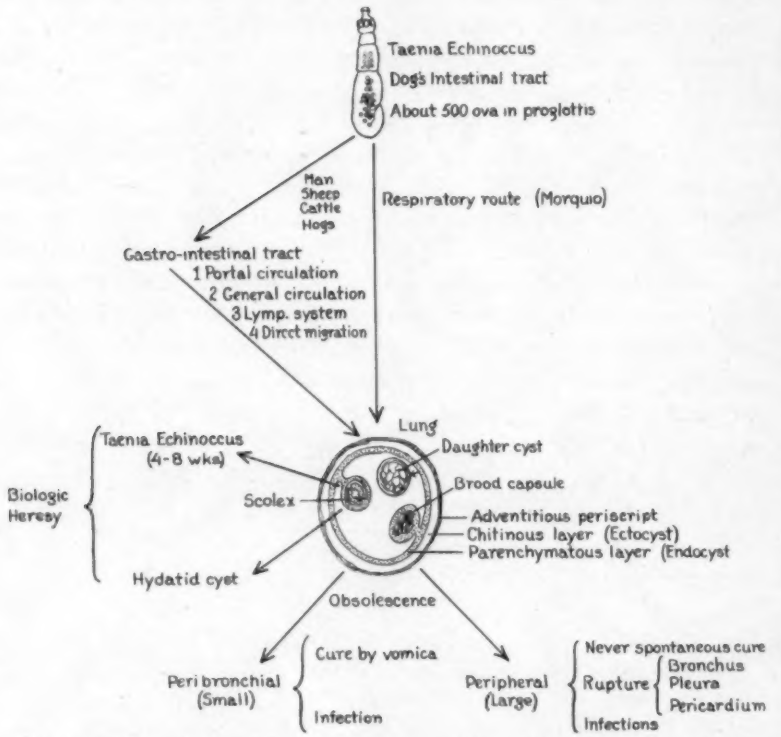

Fig. 1.—Schematic representation of the evolution of a pulmonary hydatid cyst.

be expectorated. Infection usually follows rupture, and the picture becomes that of a bronchopulmonary suppuration with cough, purulent, foul-smelling expectoration, and the evidences of sepsis.

DIAGNOSIS

It is not surprising that many hydatid cysts are discovered at operation, the true nature of the pathologic process being unsuspected until some of the characteristic elements of the cyst are found. This is especially true in countries where the disease is rare and the possibilities of such a diagnosis are not kept constantly in mind. In the Mel-

bourne Hospital, according to Strawell, the diagnosis has been reduced to a 2 per cent error. This has been made possible by constantly considering this disease in differential diagnosis and by the employment of proved laboratory aids. In a study of 182 cases, however, N. H. Fairley found that a positive diagnosis was made in only 40.7 per cent. This series includes cysts located in various organs, in many of which the x-ray picture is not capable of rendering such valuable information as it does in the chest.

There are no pathognomonic symptoms of an unruptured pulmonary cyst, but a careful investigation of patients presenting the common symptoms of cough, shortness of breath, pain in the chest and hemoptysis should permit a correct diagnosis in the great majority of cases. Roentgenographic and fluoroscopic study of the chest is indispensable. The characteristic rounded or oval shadows, multiple or single, with clearcut edges, are to be confused with few other pathologic pictures.

Since Ghedini, in 1907, first applied a complement-fixation test as a diagnostic aid in echinococcosis, many clinical investigators have elaborated and perfected a technic which at present is used extensively in those countries where the disease is prevalent. Weinberg added much to make the test valuable, and it is frequently referred to as the Weinberg reaction and sometimes as the Ghedini-Weinberg test. There is not complete agreement as to the specificity of this test. N. H. Fairley did not find a positive reaction in 917 cases free from hydatid infestation and concluded that the complement-fixation test is absolutely specific. Le Nouene [32] quoted Tuffier and Deve as reporting positive reactions when echinococcus disease did not exist. Cottin and Saloz [33] reported a case of cancer of the liver in which a positive reaction was obtained to the echinococcus complement-fixation test. It seems safe to conclude that, though it may not be absolutely specific, the percentage of false positive reactions is so slight as to be negligible. In table 1, some of the results of the complement-fixation test are listed.

The intradermal skin test, commonly called the Casoni test after the originator, also has given excellent results as a diagnostic aid. It too apparently lacks absolute specificity. K. D. Fairley,[34] in a study of eighty-seven positive reactions, was able to prove the presence of hydatid disease in only 59.8 per cent, and he said that a positive reaction is not conclusive. Ferdández Ithurrat warned that the test may be positive in tuberculosis and in patients with a highly sensitive skin. In

32. Le Nouene, Julien: A Clinical Study on Hydatid Pseudotuberculosis of the Peritoneum, Internat. Clin. **2**:97, 1921.

33. Cottin and Saloz: Reactions in Echinococcus Disease, Arch. d. mal. de l'app. digestif **13**:1, 1923.

34. Fairley, K. D.: Intradermal Test in Hydatid Disease, M. J. Australia **1**:472, 1929.

performing the test, he used from 0.2 to 0.6 cc. of sterile centrifugated hydatid fluid (human, cattle or sheep), injecting it into the skin. Within a few minutes an erythema appears at the site of injection which spreads for one-half hour or longer. In from ten to fifteen minutes, an urticarial patch about 3 cm. in diameter appears. Sette [35] prepared material for the intradermal test by evaporating 150 cc. of hydatid fluid and mixing the residue with 10 cc. of 0.9 per cent sodium

TABLE 1.—*Complement-Fixation Test*

Author	Number of Cases	Percentage of Positive Tests	Comment
Weinberg, in Kolle and Wassermann: Handbuch der pathologischen Mikroorganismen, ed. 2, 1912, vol. 1	306	82.0	
Zapelloni, quoted by Fairley[2]	500	93.0	
Fairley[2]	83	84.3	Reaction absolutely specific
Cignozzi: Riforma med. **38**: 485, 1922	...	93.0	
Ithurrat: J. A. M. A. **79**: 2018 (Dec. 9) 1922	137	88.0	
Greenway[16]	...	65.0	
Prado: Arch. de clin. méd. **1**: 1, 1925	48	92.31	
Lozano: J. A. M. A. **80**: 1533 (May 26) 1923	...	....	Weinberg test never fails him
Mogena: Arch. españ. de enf. del oparato digestivo **7**: 345, 1924	14	73.0	
Horowitz-Wlassowa: Deutsche med. Wchnschr. **52**: 113, 1926	20	90.0	Negative in 62 controls
Dew; Kelloway and Williams: M. J. Australia **1**: 471, 1925	...	92.0	
Cantani: Riforma med. **45**: 1577, 1929	...	....	A low percentage of error

TABLE 2.—*Casoni Intradermal Skin Test*

Author	Number of Cases	Percentage of Positive Tests	Comment
Mogena: Arch. españ. de enf. del oparato digestivo **7**: 345, 1924	14	100.0	
Trenti: Policlinico **31**: 353, 1924	..	....	Superior to other biologic tests
Deusch: Deutsche med. Wchnschr. **51**: 1305, 1925	..	....	Much more dependable than complement-fixation test
Finochietto: J. A. M. A. **82**: 1376 (April 26) 1924	..	90.0	
Makkas and Assimakopoulas: Zentralbl. f. Chir. **55**: 1793, 1928	61	91.8	Uncomplicated cysts
Fairley [34]	13	53.8	Suppurative cysts
	..	77.0	Uncomplicated cysts
Cignozzi: Riforma med. **38**: 485, 1922	..	92.6	Ruptured or suppurative cysts
Itharrut: J. A. M. A. **79**: 2018 (Dec. 9) 1922	..	90.0	
Dew: Brit. M. J. **1**: 673, 1927	..	98.46	
	..	90.0	

chloride and 20 cc. of glycerol. He used 0.1. cc. of this preparation in performing the test. Some of the results obtained with the intradermal test are given in table 2.

Magath found that three patients proved by operation to have hydatid cysts reacted posively to a skin hypersensitivity test. He made three small abrasions in the skin on two of which he placed hydatid fluid from a patient or from a sheep leaving the third abrasion for a

35. Sette, N.: Intradermal Test for Hydatid Disease, Policlinico **32**:1175, 1925.

control. Within twenty minutes a raised white wheal appeared surrounded by a zone of redness. There was no itching. The lesions subsided in about three hours. This test seems simple, rapid and readily interpreted and should prove to be a help in the diagnosis of hydatid disease.

A satisfactory result of any of the biologic tests used to aid in the diagnosis of echinococcosis depends entirely on the activity of the material with which the test is performed. A laboratory with an abundance of hydatid cysts passing through it can be sure of having satisfactory hydatid antigen. In this country, where only an occasional hydatid cyst is seen, most localities are not equipped to perform these tests properly. Horowitz-Wlassowa said that the hydatid antigen spoils in from four to five months. Settle claimed that by the method he uses in preparation, material for intradermic tests will keep active for as long as a year.

The significance of a positive reaction persisting after the surgical cure of a hydatid cyst has not been definitely determined. Weinberg [36] stated that "the specific antibodies disappear slowly from the blood stream of patients operated upon for hydatid cysts." He found a positive reaction up to six years and three months after operation, but admitted that the interpretation should be reserved when the reaction is positive after several years. Le Nouene quoted Laubry and Parou to the effect that the antibody disappears from the blood in from three weeks to six months after the removal of the cyst, and that a persistence of a positive reaction after six months means that a cyst has been overlooked or that there is a recurrence. N. H. Fairley regarded a strongly positive reaction after twelve months as absolutely diagnostic of another cyst. Kelloway [37] expressed the opinion that with the Casoni test both immediate and delayed reactions would continue for years following the death or surgical cure of the parasite. Deusch also said that the Casoni test remains positive for a long time after the removal of the cyst. The statement has been made by Dew, Kelloway and Williams that the complement-fixation test may be positive in cured patients sixteen years after operation.

While an increase in the number of eosinophil leukocytes in the circulating blood may occur in hydatid disease, eosinophilia does not exist often enough to be of any considerable value in the differential diagnosis. K. D. Fairley [20] spoke of it as inconstant. Cantani said that eosinophilia in hydatid disease is inconstant and lacks specificity. Mogena found eosinophilia in 54 per cent of fourteen cases. Eosinophilia in from 60 to 80 per cent was reported by Cignozzi.

36. Weinberg, quoted by Le Nouene (footnote 32).

37. Kelloway, C. H.: Symposium on Hydatid Disease, Brit. M. J. **1**:673, 1927.

Following the rupture of a pulmonary hydatid cyst, the so-called complicated cyst, additional diagnostic aids are available. The story told by the patient should frequently excite suspicion. Following a chronic cough, probably associated with hemoptysis and possibly with pain in the chest, the patient, during a coughing spell, finds the air passages flooded with a profuse watery expectoration which has a salty taste. Portions of the wall of the cyst or some of the contents of the cyst may be found in the sputum when there has been rupture into a bronchus. Probably hooklets from degenerated scolices are the commonest hydatid elements found in the sputum. However, daughter cysts and pieces of the wall of the cyst have been expectorated. Fragments of the wall, because of inherent elasticity, tend to curl up and assume a shape which has led them to be called daughter cysts. Lavillat reported a patient who coughed up "grape skins," but at operation no daughter cysts were found within the mother cyst. When communication has been established with the air passages, air may enter the cyst, giving the picture described as a "pneumocyst." If the cyst has not completely emptied its contents, a fluid level will be observed on the x-ray film. Rupture into the pleura may give the appearance of pleurisy with effusion, and if rupture into a bronchus has been simultaneous, air may enter the pleural cavity, giving the picture of hydropneumothorax. Deve [38] collected and reported a series of thirty-one cases with this complication. As shown later, the consensus condemns exploratory puncture as a diagnostic measure in hydatid disease, but in cases seen for the first time following rupture into the pleura, with the appearance of a hydrothorax or a hydropneumothorax, exploration with a needle seems a logical step. On the recovery of a fluid "limpid, like spring water" or resembling cerebrospinal fluid, the diagnosis of a hydatid cyst should be considered. Microscopic examination of the fluid may reveal scolices or hooklets. When infection has supervened, the case resembles a bronchopulmonary suppuration and becomes more difficult of diagnosis, although a search of the sputum may reveal the characteristic hydatid elements.

As one reads the reports of cases of pulmonary cysts, it is seen that exploratory aspiration for diagnostic purposes is resorted to fairly frequently. The expressions from those having the greatest experience in hydatid disease universally disapprove of this step. Dew [27] said that the exploratory puncture is rarely practiced now. He warned that it may be followed by a secondary sowing of cysts, and that the exploratory puncture of even a small cyst is dangerous. McKay [39] stated that

38. Deve, F.: Hydatid Gas Cyst of the Lung, Rev. de chir. **63**:245, 1925.

39. McKay, W. J. S.: Hydatid Cysts of the Lung and Their Surgical Treatment, M. J. Australia **1**:7, 1926.

the use of a needle and syringe must be forbidden because of the danger of infecting the cyst. Lavillat condemned the exploratory puncture. He said that it may provoke a violent anaphylactic intoxication with rapid death. K. D. Fairley [20] emphasized the danger of exploratory aspiration.

TREATMENT

There is no medical treatment for pulmonary hydatidosis. Various chemical substances have been tried, both clinically and in experimental animals, without demonstrating any value. Lolli [40] showed by his experiments in rabbits that neoarsphenamine does not influence in the least the course of echinococcus disease. He stated that no therapy, unless its efficacy has been proved in animal experimentation, should replace surgical intervention. Morquio said that medical treatment is of no avail. Deve [41] asserted that vaccination therapy, as advocated by Petroff, is ineffectual. Claims have been made that the effect of the roentgen rays is beneficial. Deve and Billiard [42] concluded from their experience in its clinical use and in experimentation with laboratory animal infestations that roentgentherapy has no curative action. In Balboni's [43] second case no change in symptoms, roentgen appearance or in the complement-fixation test followed roentgenotherapy.

Expectant treatment, because of the possibility or likelihood of spontaneous cure, apparently is a debated question. Morquio said that expectant treatment is preferable, and that most cases of hydatid cyst in the lungs of children are cured by vomica. In his experience, in 90 per cent of the cases in which rupture into a bronchus occurs spontaneously the patients recover. Deve advised watchful waiting if the cysts are small and deep in the region of the hilus or if there has been a vomica. He also said that 90 per cent of cysts rupturing into a bronchus will terminate in recovery. Pereyra [44] reported the cure of six of seven pulmonary cysts through spontaneous evacuation. Corvetto [45] collected in Lima, Peru, thirteen instances of pulmonary cysts in eight of which the patients coughed up the membrane and were cured; two were cured by operation, and three died. On the other

40. Lolli, G.: Medical Treatment of Echinococcus Cyst, Policlinico (sez. med.) **36**:601, 1929.

41. Deve, F.: Vaccination Not Effectual in Echinococcosis, Compt. rend. Soc. de biol. **91**:933, 1924.

42. Deve, F., and Billiard, A.: Hydatid Cysts and Radiotherapy, Compt. rend. Soc. de biol. **91**:848, 1924.

43. Balboni, G. M.: Hydatid Cyst of the Lung, Boston M. & S. J. **187**:879, 1922.

44. Pereyra, E. P.: Arch. latino-am. de pediat. **17**:1, 1923.

45. Corvetto, A.: Parasitic Disease of Lungs in Peru, An. de Fac. de med., Montevideo **5**:196, 1922.

hand, Dew [27] said that all patients with hydatid cysts should be operated on as soon as a diagnosis is made. Bird stated that operation is the only treatment. Prat [46] warned not to rely too much on the possibility of cure by vomica, as it occurred only twice in his forty-three cases. From a study of the various opinions expressed regarding the indications for operation, it would seem that small central cysts warrant a policy of watchful waiting, but that peripheral cysts of any considerable size require surgical intervention without too long a delay.

Therapeutic aspiration is reported by Miraillie [47] to be a dangerous procedure. He collected forty-three cases in which aspiration was employed. There were two cures, twenty-two deaths and ten negative results. The dangers incident to aspiration were discussed under diagnosis. It is safe to assume that the puncture of a hydatid cyst is contraindicated until the cyst has been exposed at operation and the field has been properly protected so as to prevent leakage of hydatid fluid into the pleural cavity.

The plan of surgical attack in pulmonary hydatid cysts must be varied so as to meet the condition of the cyst when it comes to operation. The uncomplicated cyst is an entirely different problem from the cyst that has ruptured into a bronchus and is secondarily infected. Complete agreement does not exist as to the best method of surgical treatment in the case of unruptured cyst. Syme [48] said that the ideal treatment is complete extirpation of the cyst and closure of the chest without drainage. Finochietto [49] stated that uncomplicated cysts may be removed and the wound closed without drainage. He quoted Pasados as having reported seventeen cases in which operation was performed in this manner in 1898. He never operates in two stages and empties the cyst by holding the wall of the cyst outside of the chest cavity because of the danger of secondary hydatidosis when one scolex or several remain behind. Local anesthesia is advocated by Finochietto. Bird operates in one stage, and after the removal of the endocyst depends on the condition of the adventitious pericyst for the indications for drainage. If there is no adventitious layer he closes the lung and chest without drainage. When the cavity is held open by thickening of the pericystic layer, he employs drainage for forty-eight hours. In cases with a thick adventitia, he sutures it to the pleura and drains until the cavity is obliterated. Nassetti [50] closes the chest without drainage after obliter-

46. Prat, D.: Curative Vomica in Hydatid Cyst of the Lungs, An. de Fac. de med., Montevideo **10**:161, 1925.

47. Miraillie, quoted by Crow, L. B.: Am. J. Roentgenol. **5**:513, 1918.

48. Syme, George: Symposium on Hydatid Disease, Brit. M. J. **1**:673, 1927.

49. Finochietto, E., cited in, Foreign Letters (Madrid), J. A. M. A. **82**:1376 (April 26) 1924.

50. Nassetti, F.: Treatment of Hydatid Cyst Without Drainage, Arch. ital. di chir. **12**:125, 1925.

ating the cavity within the lung by drawing the walls together with sutures. K. D. Fairley [20] operates in one stage and sutures the pleural layers if adhesions do not exist. McKay does not believe that a two-stage operation is advisable. He uses intratracheal anesthesia to render positive pressure. After suturing the adventitia to the edge of the wound, he opens the cyst and it is emptied of the fluid contents and the endocyst. He always drains the cavity for a short time so as to prevent occurrence of a subcutaneous emphysema. Antonucci [51] suggested the obliteration of the lung cavity by approximating the opposing walls with suture and closure of the chest wound without drainage. He then compresses the lung by an artificial pneumothorax. In 1925, Mills said that the consensus favored the use of a two-stage operation, called the Lamas-Prat-Mondino technic. This operation consists in a rib resection under local anesthesia with a tampon of iodized gauze placed against the parietal pleura as a first stage. This stage is followed in about ten days by an opening into the cyst without the use of anesthesia.

The method of injecting formaldehyde into the cyst at operation before incising it to remove the contents, as advocated by Deve, does not seem applicable to pulmonary cysts because of the dangers of flooding the bronchial tree with the solution.

Surgical measures in common use in pulmonary suppuration are found to deal satisfactorily with infected, ruptured pulmonary cysts. Harvey [52] reported a case in which he obtained a cure in an infected cyst through the use of an artificial pneumothorax. Pneumotomy with removal of the contents of the cavity and drainage until the cavity has become obliterated is the method of treatment commonly practiced. In 1898, J. B. Murphy [53] stressed that a suppurating cyst should be treated like a pulmonary abscess and opening into the lung should wait for fixation of the lung to the thoracic wall. Finochietto [49] has boldly depended on bronchial drainage after cleaning out an infected cyst cavity and completely closing the incisions in the lung and chest. When thick-walled cavities remain after prolonged drainage, some method to secure their obliteration must be attempted. Campbell [54] reported the cessation of the cough and expectoration following phrenectomy in a case in which an infected cavity remained after a two-stage operation for a suppurating hydatid cyst. K. D. Fairley [20] mentioned the necessity of removing several ribs in order to obliterate a cavity. In my first case it was necessary to unroof the cavity by removing the thickened

51. Antonucci, C.: Hydatid Cyst of the Lung, Policlinico (sez. prat.) **30**:798, 1923.

52. Harvey, Cotter: Suppurating Hydatid Disease of the Lung Cured by Artificial Pneumothorax, M. J. Australia **1**:458, 1929.

53. Murphy, J. B.: Surgery of the Lung, J. A. M. A. **31**:341 (Aug. 13) 1898.

54. Campbell, A. J.: Diaphragmatic Paralysis as a Therapeutic Measure in Intrathoracic Disease, Quart. J. Med. **21**:463, 1928.

parietal pleura and underlying adherent lung, together with the ribs and intercostal tissues. This allowed the superficial thoracic wall to drop into the pulmonary cavity, where it finally became adherent and permitted healing to take place.

PROGNOSIS

In 1882, Osler said, "The accidental ingestion of the eggs of the tiny *Taenia echinococcus* of the dog produces the most serious and fatal parasitic disease of man." Echinococcosis as a disease is responsible for a great many deaths in those portions of the world where it is common. Curran and Locke [55] made the statement that 14 per cent of the death rate in Iceland during 1917 was due to echinococcus cysts. The prognosis in pulmonary hydatid cysts depends mainly on whether or not there is multiple infestation as a complication. Solitary cysts or even the presence of multiple invasion of pulmonary tissue, provided the extent is not too great, should not carry a high mortality. Because of the increasing diagnostic aid offered by the biologic tests and the use of the fluoroscope and the roentgen rays, both for help in differentiation and for localization, pulmonary cysts do not present serious difficulties in diagnosis. The great advances made in intrathoracic surgery during the past few years has made it possible to develop surgical methods of handling hydatid cysts of the lung with a minimum of operative risk. In the series of thirty-three cases studied by K. D. Fairley,[20] death resulted in four, or 12.12 per cent. Operation was not performed in ten of these cases; there was apparent cure by vomica in eight and death in two, or a mortality of 20 per cent. There were two deaths in the twenty-two patients on whom operation was performed, giving a mortality rate of about 9 per cent. Heuer [56] quoted Garré as reporting an 80 per cent cure by open incision in a collection of ninety-nine cases, and Tuffier, who collected thirty-five cases treated by operation, reported only one death. These figures are comparable to statistics quoted by Lavillat. He mentioned that Pasquier reported recovery in 85.18 per cent and Guimbellat in 87 per cent.

REPORT OF CASES

CASE 1.—*History.*—Miss F. L., a stenographer, aged 19, was first seen at the Highland Hospital on Feb. 21, 1929. She was born in Delevan, N. Y., and at the age of about 3 years was brought to Rochester. She had never traveled out of her native state. For several years, the patient had a pet dog which during the last few months of its life suffered from some gastro-intestinal disturbance. It died suddenly during the summer of 1928, as other dogs in the same neighbor-

55. Curran, J. F., and Locke, A. W.: Echinococcus Cysts, Boston M. & S. J. **191**:932, 1924.

56. Heuer, G. J.: Surgery of the Lung, Nelson's Loose Leaf Surgery, 1927, vol. 4, pp. 5 and 584.

hood had, and its death was attributed to poisoning. The patient had had scarlet fever at 17 years of age; otherwise she had been well up to the onset of the present illness.

In February, 1928, she had an attack of pleurisy associated with fever and disability. She did not remember which side was involved. In March, there was a recurrence of pleurisy which lasted about a week. About June 1, there was another attack of pleurisy, for the treatment of which she entered the Genesee Hospital on June 11, where she remained for several days. A study of the hospital record reveals that 60 cc. of clear opalescent fluid was obtained by aspiration of the left side of the chest; the fluid was negative on culture and on inoculation into a guinea-pig. The blood showed a persistent leukocytosis of from 20,000

Fig. 2 (case 1).—Roentgenogram showing a large uncomplicated hydatid cyst in the lower part of each lung field.

to 30,000. There was no increase in eosinophils. Roentgenograms of the chest showed large oval shadows with clearcut edges in the lower part of each lung field (fig. 2). The diagnosis of pulmonary echinococcus cysts was suggested as a possibility by Dr. D. B. Jewett, because of the roentgen appearance. However, the patient was discharged from this hospital at her own request and was lost from observation by the staff.

Following discharge from the Genesee Hospital, she gradually improved, but did not entirely recover her strength. Unproductive cough persisted. About five weeks before admission to the Highland Hospital, she had a violent coughing spell, during which she coughed up a large quantity of pus and blood, with an extremely offensive odor. Since that time she had had a persistent cough, productive of about two cupfuls of very foul sputum in twenty-four hours. Associated with

these symptoms were evidences of sepsis with fever and loss of strength, appetite and weight.

Examination.—On admission to the Highland Hospital, physical examination revealed a pale, undernourished girl, obviously seriously ill. She had a distressing cough and raised much extremely foul-smelling, purulent sputum. Other than the poor general condition, nothing abnormal was found except on examination of the chest. The heart was not displaced. On the right side there was impaired resonance, front and back, in the lower portion of the chest. In the area of dulness there were diminished breath sounds. No râles could be heard. On the left side there was dulness beginning at the angle of the scapula. This changed to absolute flatness in the lower part of the chest. The breath sounds were absent over the

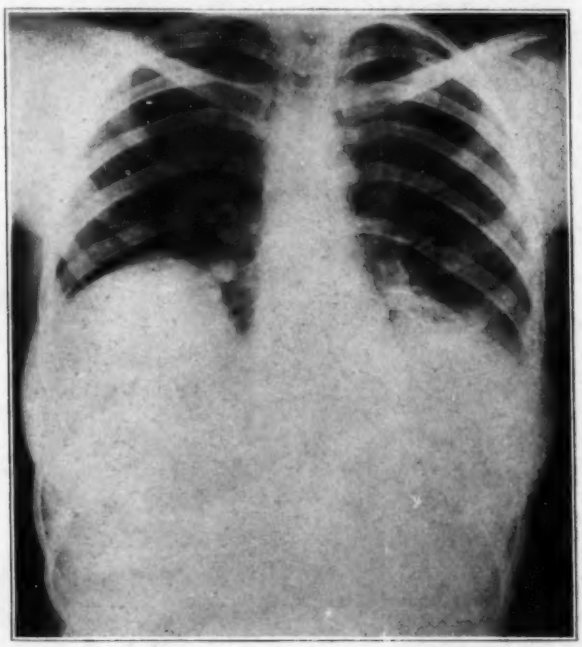

Fig. 3 (case 1).—The hydatid cyst on the left has become infected. On the right side, the shadow of the cyst merges with the diaphragm and interpretation is rendered difficult.

area of flatness and markedly diminished in the area of dulness, and there were many moist râles in this region.

Urinalysis was negative for sugar or albumin. The sputum was negative for tubercle bacilli. No search was made for hydatid elements. The blood count showed leukocytosis without eosinophilia.

Roentgenograms made at this time differed markedly from those made about seven and a half months previously at the Genesee Hospital. (It was not my privilege to study the earlier films until after I had operated on this patient.) On the left side, there was complete obliteration of the lower portion of the lung field by a uniform shadow. On the right, there was obliteration of the lower portion of the lung field by a shadow consistent with a high placed diaphragm (fig. 3). Iodized poppy seed oil 40 per cent injected into the lower portion of the

left lung field showed an uneven distribution of the material, which did not suggest bronchiectasis, but rather that the oil had entered an abscess cavity and was mixed with its contents (fig. 4).

Operations. Course.—On Feb. 22, 1929, with the patient under procaine hydrochloride anesthesia, a subperiosteal resection of about 3 inches (7.6 cm.) of the left tenth rib posteriorly was performed. The parietal pleura was thickened and hard. Careful dissection through it resulted in entrance into pulmonary tissue, showing the parietal and visceral layers of the pleura firmly adherent. On aspiration of the indurated lung, pus was recovered about 1½ inches (3.7 cm.) from the surface. The intrapulmonary cavity was opened with the cautery. There was a cavity about the size of a large orange which contained pus of extremely offensive

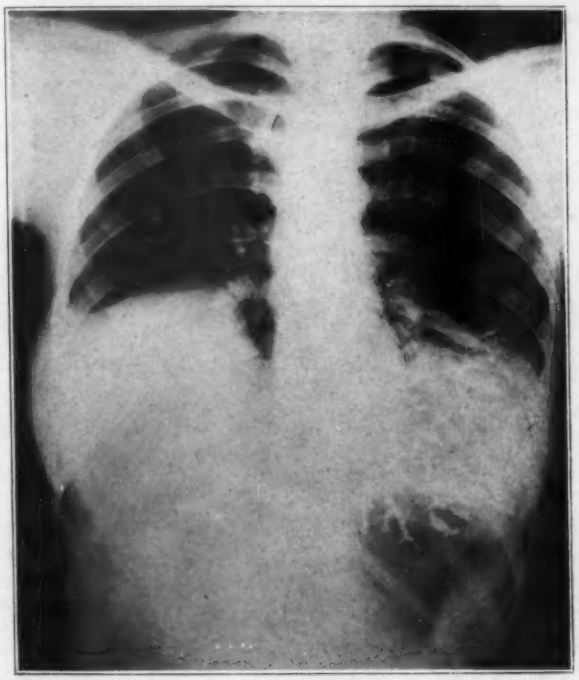

Fig. 4 (case 1).—The distribution of iodized oil through the area of suppuration in the left base.

odor that quickly permeated the entire operating floor. Further exploration of the cavity revealed that it contained a large amount of partially degenerated membrane and small circular pieces of a similar nature—all collapsed and not unlike empty grapeskins. The cavity was thoroughly emptied and drainage tubes were inserted. The external wound was held open by a gauze pack. Hooklets of the echinococcus scolex were found in the pus from the cavity.

Following operation, there was rapid improvement in the patient's general condition. The cough and expectoration disappeared. There was progressive gain in weight and strength. However, after several months' observation, there was apparently no reduction in the size of the intrapulmonary cavity and the persistence of many open bronchi annoyed the patient. It finally became obvious that spon-

taneous obliteration of this cavity was not going to take place, and the patient was admitted to the Rochester General Hospital on July 7, for treatment of the residual cavity and bronchial fistulas.

On July 8, with the patient under procaine hydrochloride anesthesia, a plastic operation designed to obliterate the remaining thick-walled intrapulmonary cavity was performed. A curved incision with convexity downward passing at lowermost limits about 3 inches below the scar and sinus of former operation was made. The skin and superficial thoracic wall were dissected upward forming a flap. The external wall of the cavity, consisting of ribs, intercostal bundles, thickened parietal and visceral pleurae and the fibrosed pulmonary tissue, was excised to the limits of the cavity. The skin flap was allowed to fall into the cavity, over the bronchial fistulas, and was held in place by a gauze pack.

Following this operation, healing was slow, but finally the skin flap became adherent to the surface of the lung. The open bronchi were frequently cauterized

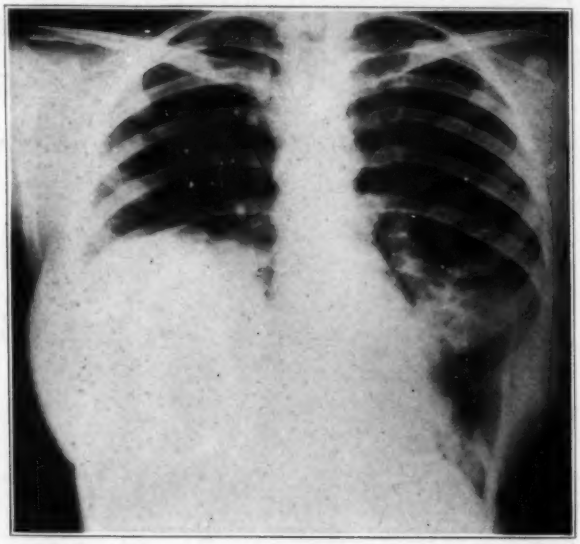

Fig. 5 (case 1).—The deformity of the lower left side of the chest resulting from operations. The shadow of the cyst on the right is still consistent with a shadow cast by a high diaphragm.

with silver nitrate during this period. During December, the healing was complete, and the bronchial fistulas were all closed. Roentgen study at this time showed deformity of the wall of the lower left part of the chest, but it was felt that there was sufficient functioning pulmonary tissue on the left side to warrant an open operation on the right side of the chest for removal of the hydatid cyst in the lower part of the right lung, which had remained unruptured and uninfected (fig. 5).

On Jan. 16, 1930, with the patient under gas-oxygen anesthesia supplemented with local infiltration and nerve block with procaine hydrochloride, about 8 inches (20.3 cm.) of the right eighth rib was resected subperiosteally. The pleura was incised, and the chest was opened for the full length of the incision. The seventh rib was sectioned at the anterior and posterior ends of the incision to obtain a better exposure. There were a few stringlike adhesions between the visceral and

parietal pleurae, and a small amount of lymph was present on the pleural surfaces. The upper and middle lobes were pink and normal in appearance. In the lower lobe of the lung there was a mass larger than a child's head, shaped somewhat like a football. It was firm and tense. Where it approached the surface of the lung it was white and cartilaginous in appearance. The lung overlying the cyst was of a deep wine-red color, almost a purple. The chest was carefully walled off with gauze packs, and the cyst was aspirated and emptied of its fluid content through a gallbladder trocar. The fluid was perfectly clear and resembled "spring-water." As the cyst emptied, the lung was grasped with clamps and delivered from the chest. An incision was made through the pericystic layer, and the hydatid cyst was removed by grasping it with sponge forceps. It was lying free within the pericyst without connections or adhesions to the host. The cavity within

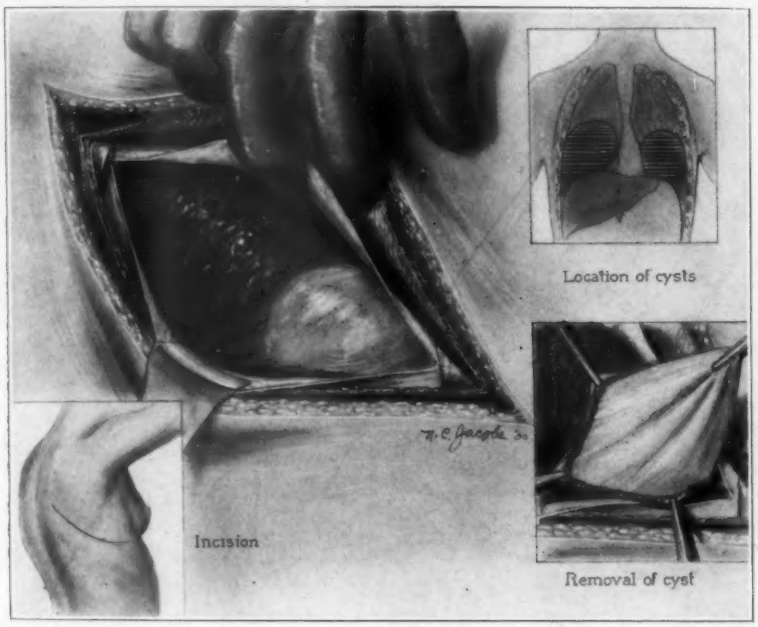

Fig. 6 (case 1).—Transpleural approach to a large cyst in the right lower lobe.

the lung was carefully cleaned out by aspiration and sponging, and through the incision into it, was marsupialized to the skin. The remainder of the incision in the chest was closed by suture in layers, resulting in air-tight closure. The operation was well borne (fig. 6).

No daughter cysts were found. The fluid from the cyst contained many brood capsules, scolices and hooklets (fig. 7).

For the first few days, the patient was moderately dyspneic, and there was slight cyanosis. There was only a moderate elevation of temperature, but the pulse rate varied between 120 and 140 for several days. There was a slight amount of bloody drainage from the marsupialized area, and for about four weeks the patient could express air from the cavity within the lung on cough or deep breathing. The incision healed without infection. After three weeks she began

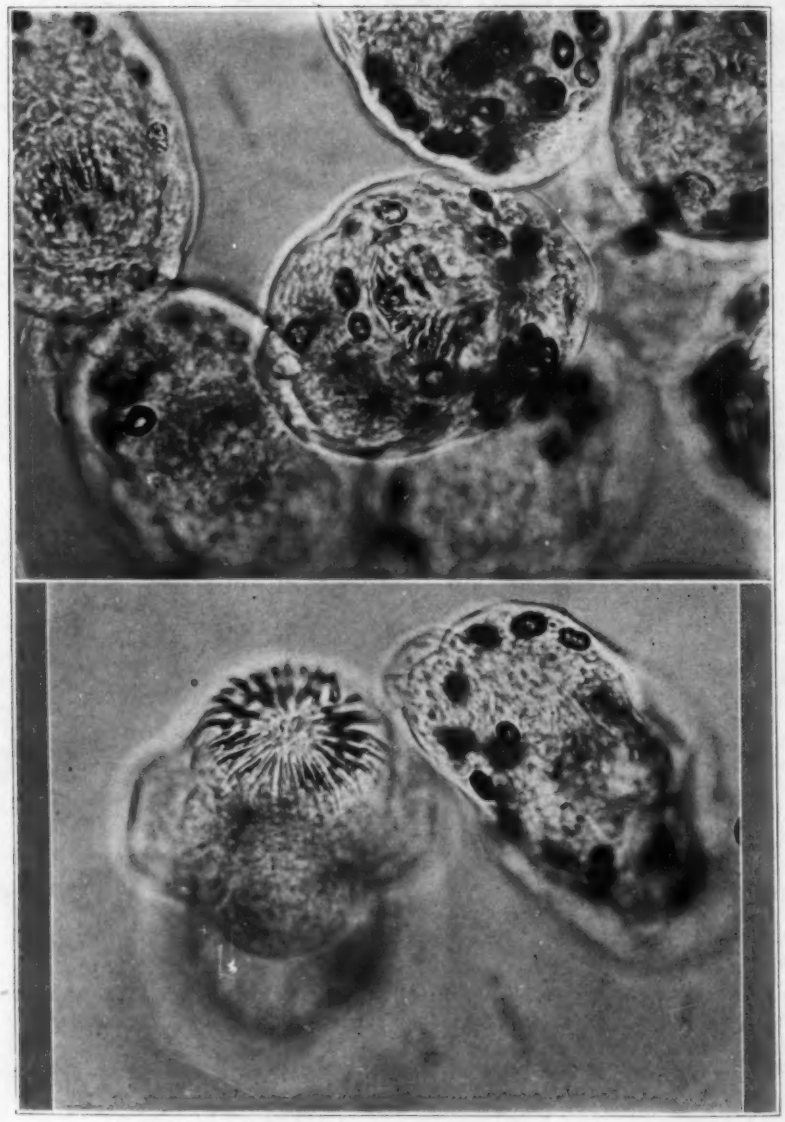

Fig. 7 (case 1).—Scolices found in the fluid from the cyst in the right lower lobe.

Fig. 8 (case 1).—Both sides healed. Shows the defect of the lower left wall of the chest.

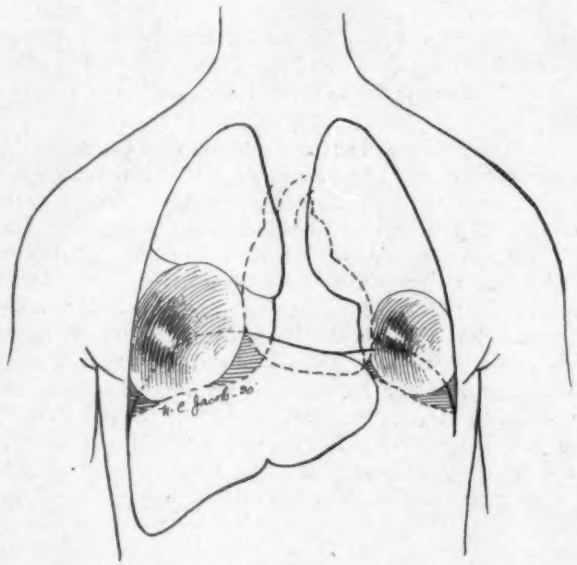

Fig. 9 (case 1).—Diagrammatic representation of the relative position of the hydatid cysts.

to get up out of bed. At first there was some dyspnea on exertion, but this gradually cleared up, so that at present she has no shortness of breath. She has progressively gained in strength and weight (fig. 8).

About two months after the last operation, an intradermal skin test performed with echinococcus antigen prepared from the contents of the patient's hydatid cyst provoked no immediate reaction, but there was a delayed reaction in the form of an erythematous area about 4 cm. in diameter, which appeared in about eighteen hours and persisted for two days.

Summary.—A large hydatid cyst was present in the lower lobe of each lung. The cyst on the left side ruptured into the bronchial tree and became infected. The suppurating cyst was removed through pneumotomy, and a secondary plastic operation was necessary to obliterate the residual fibrosed lung cavity. The cyst on the right remained unruptured and did not become infected. It was removed by a one-stage operation, and recovery followed.

Dr. James M. Markin of Rochester referred this patient to me (fig. 9).

CASE 2.—*History.*—Mr. B. A., an Italian, aged 35, was admitted to the Rochester General Hospital on Dec. 9, 1927, because of pain in the right side of the chest, cough and hemoptysis. In Italy, he had lived on a farm and had tended sheep and cattle. He had a dog at that time. He came to the United States about sixteen years ago. During the World War, he served with the army in France for about nine months. He had scarlet fever while in Italy, but aside from this had been well until the onset of his present symptoms. For about ten years he had had pain in the right side of the chest and a chronic cough. There had been some expectoration, at times of a black color. Occasionally he had noticed blood in the sputum. He had had some dyspnea, and occasionally suffered from night sweats. His appetite was good, and he had not lost weight. About one week before admission to the hospital, he felt feverish and had increased dyspnea. He consulted his physician, who found a large shadow in the right side of the chest on fluoroscopic examination, and the patient was sent to the hospital for study and treatment.

Examination.—The patient was an obese Italian. The temperature on admission was 101 F., pulse rate, 98, and respiratory rate, 22. Nothing abnormal was found on examination except for the chest. There was no bulging or retraction of the thoracic wall. The expansion was limited over the right side. The percussion note was dull over the right side of the chest, especially posteriorly. Over the back, the breath sounds were absent, and they were considerably diminished in the axilla and over the front of the right side of the chest. There were no râles. The left lung was clear throughout. The heart was not displaced; the heart sounds were of fairly good quality and there were no murmurs.

Urinalysis gave entirely negative results. The red blood count was 4,630,000, and the hemoglobin reading, 91 per cent (Sahli). The white blood count was 8,300; polymorphonuclears, 70 per cent; lymphocytes, 27 per cent; transitionals, 2 per cent, and eosinophils, 1 per cent. The Wassermann and Kahn reactions of the blood were negative. Roentgen examination was performed by Dr. L. R. Lingeman, who reported a large dense shadow occupying the lateral aspect of the right thoracic cavity. This had a sharp, clearcut medial margin and a homogeneous density throughout. He felt that it was necessary to consider in the differential diagnosis, a large encysted pleural effusion, a malignant condition of the pleura and echinococcus cyst of the lung (fig. 10).

An intradermal injection of an echinococcus filtrate caused no reaction, either immediate or delayed. (This filtrate was about a year old and I have no knowl-

edge as to its antigenic content. Presumably it had lost the power of provoking a reaction.)

Operation.—On December 12, with the patient under gas-oxygen anesthesia supplemented with infiltration and nerve block with procaine hydrochloride, a long segment of the right ninth rib was excised. Many adhesions existed between the lung and the parietal pleura, which were separated by finger dissection. There was a large cystic tumor in the right lower lobe reaching from the diaphragm high into the chest. The external wall of the cyst was thick and fibrous and showed some calcification. The cyst was aspirated, and grayish-red fluid was obtained. It gave somewhat the appearance of a suspension of gold-dust. The

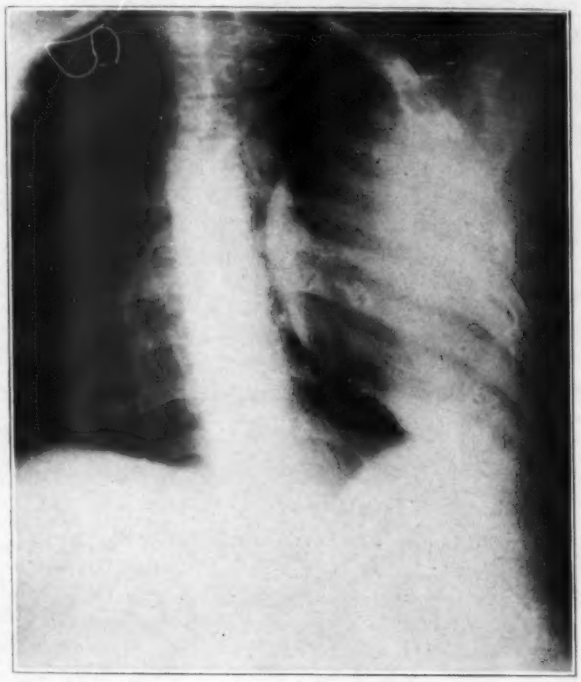

Fig. 10 (case 2).—Roentgenogram showing large, dead cyst of right lower lobe.

wall of the cyst was incised, and a large amount of the same fluid escaped, together with degenerated tissue not unlike fibrin. The external wall of the cyst was excised as far as it could be reached. There was no evidence of open bronchi on the inner wall of the cyst. The cavity was packed with gauze, soaked in acriflavine 1 : 500, and the anterior end of the incision was closed in layers.

Pathologic Report.—The fluid and pieces of the wall of the cyst were examined by Dr. I. Gaspar, who reported that the fluid contained many cholesterol crystals. Several smears of the centrifugated sediment were examined, but no hooklets were found. Section of the wall of the cyst showed a marked hyaline fibrosis. There were no bronchial glands and no deposit of hemosiderin pigment in the wall. He concluded that the etiology of the cyst could not be definitely determined, but it is possible that it was a fairly old echinococcus cyst.

Course.—The postoperative period was complicated by a prolonged febrile reaction. Immediately following operation, the temperature rose, fluctuating between 102 and 103 F. and remained at this level for ten days, when it increased to between 103 and 105 F.; it persisted at this height until the nineteenth day, when it fell to between 100 and 101 F., at which level it continued for several weeks. During this time the pulse ranged from 110 to 130. This was thought to be the result of infection in the pleural cavity. The drainage from the chest became purulent and rather foul. Following the institution of irrigation with surgical solution of chlorinated soda (Dakin's solution), the foul odor disappeared and the nature of the drainage changed. A transfusion of 500 cc. of citrated blood was given once following operation, as the red blood cells had fallen to 3,720,000 with a hemoglobin reading of 71 per cent. On Jan. 12, 1930, the cavity within the chest held 500 cc. of surgical solution of chlorinated soda. The use of "blow-bottles" was started, and the patient was encouraged to use them frequently. By February 9, the size of the cavity had decreased so that it overflowed on instillation of 185 cc. of the surgical solution. On February 13, it was necessary to enlarge the sinus tract under local anesthesia as the tract had become so narrowed as to prevent adequate drainage. Serial roentgenograms showed a progressive, although slow, decrease in the size of the residual cavity. On April 17, a roentgenogram showed only a narrow unobliterated cavity. The lung showed definite expansion. The cavity held but 45 cc. on April 30. The patient's general condition remains excellent.

Summary.—The patient presented a large cyst in the right side of the chest. It was treated surgically by removal of the contents and excision of the greater part of the external wall. There were no scolices or hooklets found in the cyst's contents. I believe that this case represents one of a large hydatid cyst which had terminated its growth by obsolescence. In favor of this opinion are the long course of the typical symptoms of a hydatid cyst of the lung, the roentgenologic appearance and the operative observations, all of which are difficult to explain on any other basis.

CASES REPORTED IN THE LITERATURE

GAY'S CASE[57] (1858).—D. R., a man, aged 71, had always been well until February, 1857. The symptoms in the illness preceding his death were entirely bladder difficulties. There was no mention of pulmonary symptoms or signs. Autopsy showed a carcinoma of the bladder. "At the apex of the left lung was a layer of white, dense, fibrous tissue an inch in diameter, and between one or two lines in thickness. The surface in the immediate neighborhood was rendered opaque, with thin patches of the same. Beneath a dense white substance was a layer of pulmonary tissue of about the same thickness, and within this a cavity upwards of ½ inch in diameter filled with serum and lined by a thin bluish-white membrane which was everywhere studded with yellowish-white points. Most of the serous fluid was lost. That which remained was of a yellowish color and contained a large number of echinococci, detached hooks and a few concentric corpuscles. The lining membrane itself was covered with the same parasites. It presented the usual striated appearance."

Summary.—A man, aged 71, died from carcinoma of the bladder. Autopsy revealed a hydatid cyst of the left lung unrecognized during life. The diagnosis was proved by recovery of hooklets and echinococci.

57. Gay: Case Report, Boston M. & S. J. **57**:218, 1858.

STILLE'S CASE [58] (Credited to Gay by Lyon).—At a meeting of the Pathological Society of Philadelphia, a cyst was exhibited about three-fourth inch (1.8 cm.) in length, pyriform and containing yellowish-red fluid. This was expectorated shortly before death by a man whose main symptoms were great emaciation and cough, and who presented dulness on percussion and a feeble respiratory murmur of the right lung, at the apex of which gurgling also existed. There was no postmortem examination and no proof as to the nature of the cyst.

Summary.—A cyst was expectorated shortly before death by a man presenting pulmonary symptoms. This case is included by Lyon in his series as a pulmonary hydatid cyst. The record makes acception questionable.

SMITH'S CASE [59] (1858).—Mrs. A., aged 34, from girlhood had had symptoms of a diseased liver. At intervals of one or two years there were acute paroxysms of pain accompanied by enlargement. In the winter of 1857, growing tenderness was noted in the hypochondriac region. The side was swollen even to distortion of the ribs. Much pain and numbness in the arm and foot of the right side were constant symptoms. Early in April, 1857, the disease became more acute. The swelling of the side, the pain and the soreness increased rapidly. There was great pain in the top of the head with acceleration of the pulse. Without premonitory symptoms of any kind, there was a large discharge from the bowels of fetid, purulent and bloody matter which continued for two and a half days, producing great exhaustion. Cough set in with expectoration of frothy fluid at first, and later sputum resembling that of pneumonia. About September 1, cysts were first coughed up, from one to three in a day, varying in size from that of a filbert to that of a pea, all much torn. They were examined by more than one observer, and not a trace of parasite was found. The discharge of cysts became gradually less frequent but more numerous and more variable in size. Sometimes after an interval of five days, twenty or thirty would be thrown off at one paroxysm of coughing that lasted two or three hours. Later these paroxysms occurred once in ten days, and the cysts were discharged perhaps during the course of two days. Some were so perfect as to have but one aperture; they were inflated by the blow pipe. Some smaller than a pea came up unbroken, but soon collapsed. Their contents were apparently purely serous, and the same thick expectoration as at first accompanied them. The cysts were opaquely white—with few exceptions, the walls were translucent—and under the microscope exhibited only occasional striae. At the time this case was reported the patient had much less pain and suffering than she had the winter before, though she was not so strong and respiration was more deficient. The specimens of sputum contained some clots of blood. The paroxysms were exhausting, violent and spasmodic, resembling those of whooping cough.

Summary.—A woman, aged 34, whose birthplace was not mentioned, apparently had a large cyst of the liver which ruptured into the gastro-intestinal tract. There was also primary infestation of the lungs with a cyst rupturing into a bronchus and partially discharging its contents. The numbness in the arm and the foot on the right side together with the intense headache suggests also a cyst involving the central nervous system. The case was reported as "cysts from the liver coughed up through pulmonary passages." The case is included in Osler's series as an instance of echinococcus cyst of the lung.

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58. Stille: Case Report, North Am. Med. & Chir. Rev. **2**:506, 1858.

59. Smith, F. Gurney: Case Report, North Am. Med. & Chir. Rev. **2**:333, 1858.

MINOT'S CASE[60] (1859).—A woman, aged 35, for several years had had pain shooting to the back and to the right shoulder and uneasiness in the right hypochondriac region. In the spring of 1856, while in New Orleans, she was seen by a physician who detected an obscure tumor in the right hypochondriac region, which he described as feeling like a watch, deeply seated beneath the integuments. At this time she had considerable prostration. In April, 1857, a large tumor developed rapidly in the same spot. It embarrassed respiration and compressed the right side of the lung so that no respiratory murmur could be heard, except in the upper part of the right side of the chest. It was excessively painful and tender. One night she had several enormous evacuations from the bowel, the discharge being clear, colorless fluid and excessively fetid. The tumor almost wholly disappeared at once. She was extremely prostrated and had considerable fever, from which she slowly recovered. About June 1, she began to cough and to expectorate frothy mucus. About September 1, she began to cough up hydatid cysts of various sizes. This occurred about twice a week, two or three being discharged each time, with a sensation as if they were detached from the lower part of the right lung. The tumor diminished, and in October could no longer be felt. The patient's health steadily improved, and on Sept. 27, 1859, she was quite well. She had not coughed up any hydatid cysts for three months.

Summary.—A woman, aged 35, whose nationality was not known, had a large cyst in the upper right part of the abdomen which discharged into the gastrointestinal tract. Her condition was later complicated by the expectoration of hydatid cysts, over a period of many months. This case was reported by Lyon as a case of hydatid of the liver with perforation of the diaphragm and the lung. A study of the case record suggests multiple infestation of the lung and liver.

LOOMIS' CASE[61] (1878).—A man, aged 43, a native of Ireland, a shoemaker, at the age of 19 had his first attack of inflammatory rheumatism, which lasted two months and involved all of the large joints. He had several similar attacks at intervals of from one to four years. The length of attacks varied from one to three months. In September, 1867, he suffered from unusual cardiac palpitation accompanied by severe paroxysms of coughing, and for the first time in his life he raised blood. The spitting of blood continued almost without interruption until Jan. 10, 1878. The blood was bright red and varied in quantity from 1 to 2 teaspoonfuls. During this time, he raised some blood nearly every day. On January 10, he began to spit up much larger quantities than ever before. From January 10 to 18, he thought that he raised as much as 18 pints of blood. On January 18, after a violent fit of coughing, he raised something that had the appearance of a membrane. It was pearly white and partly red. Following this, he raised other pieces, some of which looked like little sacs. Each time he expectorated a piece he would spit up a large quantity of bright red blood. During the period of profuse hemorrhage, he lost weight rapidly and became very weak. Three weeks after the first profuse hemorrhage he again coughed up membrane and had another severe hemorrhage. At this time he felt as though something was torn out of the inside of his chest. The membrane came up in quite large pieces, and he experienced a sense of relief. Since then he raised no blood or membrane. At the time this case was reported he coughed a little and had a slight amount of mucopurulent expectoration. He gained steadily in weight and

60. Minot: Case Report, Boston M. &. S. J. **61**:279, 1859.

61. Loomis, A. L.: Hydatids of the Lung, M. Rec. **14**:281, 1878.

strength. Palpitation, which had troubled him more or less for the past two or three years, was less than at any time since that period.

He generally looked quite well. The pulse and temperature were normal. On examination of the chest, the right shoulder was found to be lower than the left, and there was slight retraction on the right side, more marked posteriorly than anteriorly. Motion of the right side during respiration was markedly diminished. The apex of the heart was plainly visible 1 inch (2.5 cm.) to the left of its normal position. Vocal fremitus was more marked on the right, especially in the mammary and superior axillary regions. There was loss of resonance all over the right side of the chest, being most marked in its lower portions. Exaggerated respiration was heard all over the left lung. On the right side below the nipple there was almost absence of respiratory sound. On a line with the nipple, bronchial breathing was heard over the right infraclavicular space.

There was hypertrophy of the heart with mitral regurgitation and stenosis. The lower margin of the liver was palpable below the costal margin. It was smooth and rounded. The spleen was slightly enlarged on percussion. No tumor was palpable in the abdomen. The sputum contained portions of the wall of the hydatid cyst and in some instances a complete hydatid cyst. There were minute white particles within the cyst. Under the microscope, they proved to be "echinococcus homonomous."

Dr. Loomis concluded that it was probable that at the time of his examination there were no cysts in the lungs, as the patient had had neither hemorrhage nor pulmonary symptoms since he last expectorated a cyst about four weeks before.

Summary.—A man, aged 43, a native of Ireland, suffered from cardiac hypertrophy with mitral stenosis and regurgitation. Apparently spontaneous cure occurred by rupture into the bronchus and expectoration of the cyst. However, a four weeks' follow-up seems insufficient to prove a spontaneous cure. The diagnosis was proved by microscopic discovery of "echinococci homonomous."

AINSWORTH'S CASE [62] (1880).—Max Stearns, Polish, aged 40, was admitted to the Post Hospital, Fort Vancouver, in the latter part of August, 1875. The history and physical examination gave indications only of urinary and abdominal disease. On the fourth day after admission symptoms of acute general peritonitis developed, and the patient died on September 12.

Autopsy revealed general peritonitis. The bladder was completely filled with cysts, about sixty, varying in size from that of a pinhead to that of an orange. The cysts were lying free in the bladder. They were all single. The bladder also contained a much larger sac, ruptured, which was considered to be the mother sac.

The middle lobe of the right lung contained, embedded in its anterior portion, a tumor a little larger than a walnut, consisting of a firm, fibrous, yellowish-white capsule intimately connected on all sides with the pulmonary tissue and containing several cysts varying in size from that of a pea to that of a marble. There was also a cyst in the lower extremity of the spleen about the size of an orange, similar in external appearance to the one in the lung. There is no mention of a microscopic examination.

Summary.—A man, aged 40, Polish, died of general peritonitis. No pulmonary symptoms had been noted. Hydatid cysts of the bladder, spleen and middle lobe

62. Ainsworth, F. C.: A Case of Hydatids of the Bladder, M. Rec. **18**:346, 1880.

of the right lung were found at autopsy. The diagnosis was not proved by microscopic study, but the gross description seems satisfactory proof.

FENGER AND HOLLISTER'S CASE [63] (1881).—Francesco Coputa, an Italian, aged 34, a laborer, was a patient in the Cook County Hospital. Twelve years before, while a mounted gendarme in Italy, he suffered from a hemorrhage from the lungs of about 2 ounces (56.7 Gm.). He was hospitalized for one week. During the next two years, he remained well. After this time he had a cough accompanied by pain around the right nipple. The pain subsided on the application of leeches, and the cough also disappeared after a month. In the following years, every autumn he had a return of the pain, always at the same point in the chest, between the third and fifth ribs and around the nipple, accompanied by coughing. This would persist for a month but was relieved by the use of leeches and venesection. During the past four years the pain became more severe, as did the accompanying cough. In the interval between attacks he would occasionally feel some pain in the region of the right nipple when lifting a heavy weight. He came to New York in 1870, where he stayed one and a half years. He worked during this time, except for the period in the fall in which he had his usual attack of pain and cough, during which he expectorated mucous matter which was occasionally slightly streaked with blood. In July, 1880, he came to Chicago, where he commenced work as a common laborer. During September, the pain in the right nipple set in again. It was a steady unvarying, intense pain, accompanied by a slight cough. His appetite remained good, but he was forced to stop work for two weeks. In November, he had a recurrence of pain and cough and had to stop work. He lost his appetite, became weak, and for the three weeks prior to admission to the hospital was confined to bed. During this time cough distressed him day and night, and in the twenty-four hours he raised about 1 pint of mucous matter, sometimes streaked with blood. Suddenly, about one week before entrance to the hospital, he coughed up a large quantity of whitish material, as he said, "white, like paper." Cough and pain increased. He grew weaker, lost his appetite and was unable to sleep. He was told by those about him that his breath was offensive.

Physical examination showed a poorly nourished man, tall and of moderate weight, with profuse perspiration. The pulse rate was 98, the temperature 104 F. and respiratory rate 36. When he lay on his back and the chest was percussed, he coughed incessantly, and a very offensive odor was noticed around the bed.

Percussion showed dulness below the second rib anteriorly on the right side. There was also dull percussion in the axillary and infra-axillary regions and over the scapular and interscapular regions. When the patient lay on his back, there was an area of tympanitic percussion on the anterior side of the body. Both sides of the chest participated equally in the respiratory movements. The right side of the chest was neither sunken nor prominent. The intercostal spaces had the same appearance on the right as on the left side. In the region of the dull percussion note, the tactile fremitus was nearly, but not quite, absent. Over the right side of the chest, sibilant râles were heard in the upper part of the upper lobe and in the posterior part of the lower lobe over the regions of the dull percussion; respiratory sounds were obscure. When the patient lay down, there were cavernous respiratory sounds over the tympanitic area. The anterior part of the right side of the chest near the nipple line was aspirated with the patient sitting up, and thin, grayish fluid of the same offensive odor as the breath was withdrawn. On microscopic examination, the fluid contained a large number of pus cells with fatty detritus and bacteria.

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63. Fenger, Christian; and Hollister, J. H.: Opening and Draining of Cavities in the Lungs, Am. J. M. Sc. **81**:378, 1881.

The diagnosis was fetid cavity of the middle lobe of the right lung near the anterior surface and most superficial at the nipple, having an insufficient outlet through a large bronchial tube in the anterior border of the cavity, and diffuse, purulent bronchitis in the left lung. Operation was performed by Dr. Fenger on December 26, with the patient under ether anesthesia. An incision 2½ inches (6.27 cm.) long was made in the third intercostal space, 1½ inches (3.7 cm.) to the right of the sternum. The incision was carried down, exposing the intercostal muscles. A detached hypodermic needle was introduced, and as neither inspiration nor expiration caused this to move, it was withdrawn and the incision carried into the cavity. About one-half pint of grayish-white offensive matter mixed with some air escaped. The opening was then enlarged to allow entrance of the finger into the cavity. Digital exploration revealed firm tissues toward the axilla, and in this region between the fifth and sixth ribs a counter opening was made. A heavy rubber tube, 10 mm. in diameter, was now passed from the anterior to the posterior opening. The cavity was irrigated with 2 per cent carbolic acid. As soon as the cavity was filled, the patient began to cough. During coughing it was noticed that a yellowish-white mass would appear at and protrude a little from the anterior opening. This was removed. It was one large coherent gelatinous mass. On microscopic study, this proved to be a large echinococcus cyst. The wall of the cyst presented the characteristic finely striped, that is, laminated, layers of amorphous or homogeneous substance, the stripes always running parallel to the surface of the wall. The sac was from about 5 to 6 inches (12.7 to 15.2 cm.) in diameter. The wall was homogeneous, gelatinous and transparent. It was soft and friable, but still somewhat elastic, and presented no secondary cysts. On Feb. 6, 1881, the incisions were healed, and the patient had no cough or expectoration. On April 7, he was discharged from the hospital as cured.

Summary.—An Italian, aged 34, had pulmonary symptoms of twelve years' duration. There were cough, pain in right side of the chest and hemoptysis. The cyst ruptured into a bronchus, and this was followed by suppuration within the cyst. Pneumotomy was performed, and recovery ensued. The diagnosis was proved by the microscopic examination, although there is no mention of the discovery of scolices or hooklets. This is the first recorded case of suppuration of the lung cured by pneumotomy.

SMITH'S CASE[64] (1882).—A girl, aged 20, was first seen on Nov. 4, 1881. Her chief complaint was a running sore on the posterior part of the chest. This was situated opposite the eighth intercostal space on the left side 2 inches (5 cm.) from the spine. Several sinuses were found running upward and outward. There was no other bulging on the chest. She did not have cough, pain or shortness of breath. The duration of symptoms was two years. Symptoms began with pain in the left side followed by slight shortness of breath and very little cough, but no expectoration. Occasional chills, fever and sweating were noted. After six months a tumor as large as a closed fist developed near the inferior angle of the scapula. It had been diagnosed and treated as a fatty tumor, cold abscess, etc. On two or three occasions it was opened and pus escaped. Operation was performed on November 30, with the patient under chloroform anesthesia and the sinuses were laid open by an incision extending from the sixth to the ninth ribs. A probe could be made to pass deeply through the small openings in the sixth, seventh and eighth intercostal spaces. Two transverse incisions 1½ inches long were then

64. Smith, D. F.: Case Report, Canad. M. & S. J. **11**:195, 1882.

made in the intercostal spaces, and a considerable quantity of dirty, brown pus escaped. The finger could now easily be passed through around the intercostal slit, and the costal walls of the cavity were felt to be smooth, regular and unyielding. Injection through the upper openings resulted in pus and a number of small, smooth and slippery-walled cysts of different sizes being forced through the lower opening. The cysts were all opened when they escaped, and they quite collapsed; none was larger than a marble. Some of the cysts still contained a small quantity of slimy, semitransparent, glairy fluid. No microscopic examination was made. The patient progressed well, and recovery was complete in two months.

Summary.—A girl, aged 20, presented slight pulmonary symptoms. The thoracic wall was penetrated by a suppurating cyst from within the left pleural cavity. There was no definite proof that the disease originated in the lung. It may have been a pleural cyst (fig. 11).

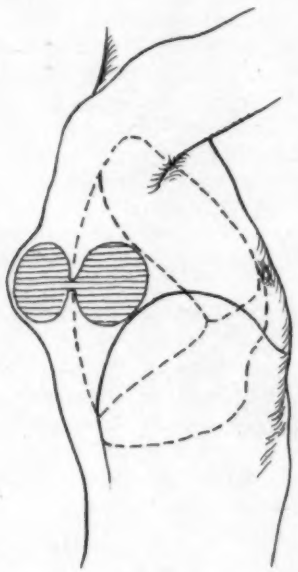

Fig. 11 (D. F. Smith's case).—Spontaneous penetration of the thoracic wall by a suppurating cyst.

BERNAY'S CASE[65] (1882).—This was the case of an Englishman, who had come from Honolulu, who expectorated an echinococcus from the lungs.

Summary.—This case was not published and was recorded in the foregoing brief manner in Osler's series of cases. Lyon credited the case to Bernay, but the reference given was to Osler's compilation of case reports, in which Bernay's case is included.

BLACK'S CASE[66] (1882).—A minister, a native of Essex County, England, had been in Canada about six years. He first consulted Dr. Black in November, 1878. He gave a history of gradually failing health for four years. In 1876, Dr. Aikins

65. Bernay: Case Report, Am. J. M. Sc. **84**:475, 1882.

66. Black: Case of Echinococcus Disease of the Lung, Canad. M. & S. J. **11**: 140, 1882.

of Toronto had discovered and removed a hydatid tumor of the liver. For a time he was improved, but the improvement was not lasting. During a year and a half prior to this consultation, he was steadily less fit for attending to his duties. The patient was much emaciated and of sallow complexion. His countenance had a pinched and somewhat cachectic appearance. He had some dyspnea with a dry cough. The epigastrium and right hypochondriac region were tense and somewhat tender. The lower intercostal spaces on the right were enlarged and tense. There was marked dulness over the lower part of the right lung. The heart was in normal position and greatly deficient in force. The spleen was slightly enlarged. The lateral margin of the liver was large, hard and smooth. There was increasing dulness in the right side of the chest. The spleen increased in size rapidly. Dyspnea became more marked. Some edema of the feet developed. On Feb. 25, 1879, after a distressing coughing fit, he raised nearly 2 pints of purulent fluid, in which floated a large number of cysts varying in size from 2 to 3 inches

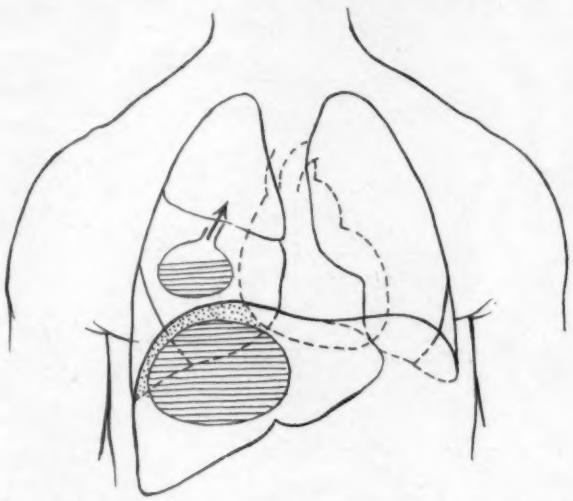

Fig. 12 (Black's case).—Cyst in the right lower lobe communicating externally through a bronchus; large unruptured cyst of the liver.

in diameter to those barely perceptible. Following this, there was daily purulent expectoration and some cysts. Gradually the symptoms improved. On March 10, he had succeeded in raising, a cyst larger than any of its predecessors. When "giving a sudden cough, purulent material began to boil out of his mouth and nostrils and he was strangulated instantly."

Autopsy revealed "abscess of the lower part of the right lung which had been distinct from that of the liver. The purulent matter and cysts discharged on February 25, and from that time until the tenth day of March, I believed to have been the contents of this abscess. The cavity was flooded by a greenish-yellow purulent fluid and floating cysts discharged from the hepatic abscess. The heart was lying with its apex to the left nearly beneath the left sternoclavicular articulation. The upper part of the right lung was studded with tuberculosis. The left lung was in its normal condition. The diaphragm was pushed far up into the thorax; the liver was adherent to the diaphragm, and through the diaphragm

was a large opening which communicated with an immense cavity in the liver. The rupture of the diaphragm and the consequent discharge of the contents of the hepatic abscess I believe to have been the immediate cause of death. The cavity in the liver was about 9½ inches in depth and 6 inches across. In the cavity was still a large quantity of greenish-yellow fluid like that found in the chest. The liver was of immense size and studded with tubercles of a yellowish color, many of which were about the size of a pea. The spleen had imbedded in it a large cyst filled with colorless fluid in which I could detect no scolex."

Summary.—A man, age not given, a native of England, had been in Canada for six years. A large hydatid cyst of the liver and a large hydatid cyst of the right lower lobe of the lung were found. The cyst of the lung ruptured and discharged through a bronchus, following suppuration. The infected cyst of the liver ruptured

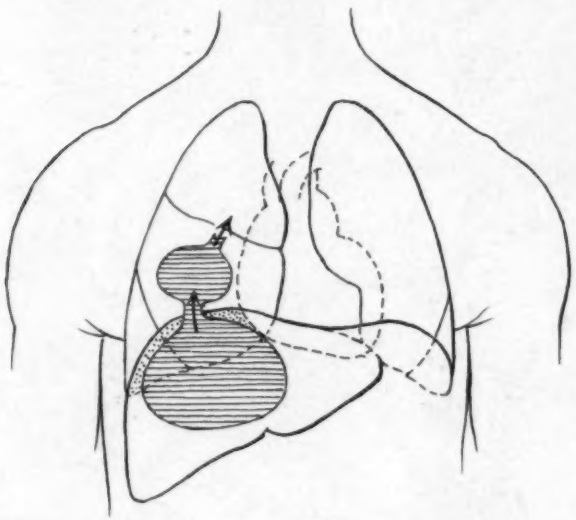

Fig. 13 (Black's case).—The cyst of the liver penetrated the diaphragm and lung, emptying into the intrapulmonary cyst and causing death.

through the diaphragm into the pulmonary cyst, causing sudden death of the patient by drowning (figs. 12 and 13).

Ferguson's Case[67] (1893).—In a patient dying from cancer of the stomach, a large cyst was discovered post mortem. "He did not complain of his lungs and a cyst, a small one, was first discovered on the postmortem table."

Summary.—A cyst of the lung was discovered at autopsy. There was no microscopic proof of the nature of the cyst. Probably Ferguson's classification of this cyst as a hydatid cyst is satisfactory proof, as he had a fairly extensive experience with hydatid infestation among immigrants from Iceland who had located in Winnipeg. He reported having seen twenty-one cases of hydatids of the liver and six others in which hydatid cysts were located in other organs.

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67. Ferguson, A. H.: Hydatids of the Liver, Northwest Lancet **13**:41, 1893.

KEYES and BUSCH'S CASE [68] (1896).—A German, aged 53, of extremely intemperate habits, had had typhoid fever in 1865 and some liver trouble in 1872, at which time, according to his statement, he passed a quantity of black marbles, probably gallstones. His last illness dated from January, 1895. On March 17, he came under the care of Dr. Hebenstreit and Dr. Meisbinger, who obtained the following history. The patient had pain in the right side near the liver. He coughed up a grayish fluid of a disagreeable odor, and an acid taste. The right side of the chest was bulging. The right pleural cavity was aspirated, and one syringeful of serous fluid was removed. A small tumorlike mass, which could be felt just below the ensiform cartilage and to the right, was also explored with a hypodermic needle with negative result. On percussion, the liver did not extend below the free border of the ribs. It extended as high as the nipple in front and at the same level to the median line behind. In the axillary line there was flatness extending to the crest of the ilium. The patient died on March 16, 1896.

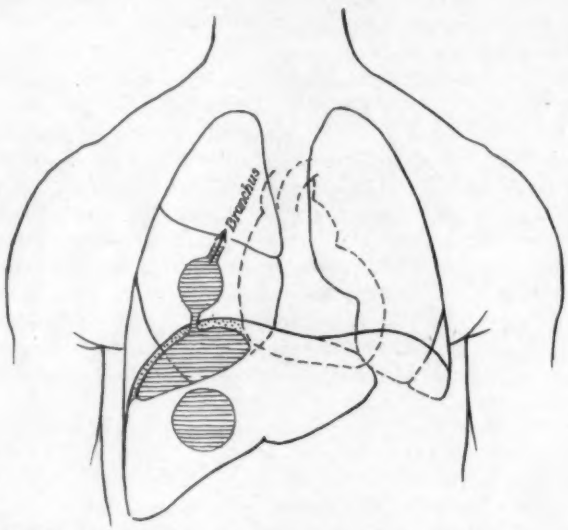

Fig. 14 (Keyes and Busch's case).—Intrapulmonary cavity communicating with a large cavity in the subphrenic region; also an unruptured cyst of the liver.

Autopsy revealed no fluid in the pleural cavities. The left lung was normal. The right lung was firmly adherent at the base to the diaphragm. It crepitated well. On section, bloody froth exuded from the bronchial tubes. A cavity with calcareous walls was discovered in the base of the lower lobe, 50 mm. in breadth and 10 mm. in depth. It communicated with the bronchus on one hand, and on the other, through an opening in the diaphragm with a similar though much larger cavity immediately below the diaphragm which measured 100 mm. in its horizontal diameter and was 15 mm. in depth. It was also lined by calcareous plates. No opening could be discovered leading from it, except that into the lung cavity. Immediately beneath this subdiaphragmatic cavity, there was still another. It was partly surrounded by liver tissue and was intimately connected to the gall-

68. Keyes, W. C., and Busch, F. C.: A Case of Multiple Echinococcus Cysts, Buffalo M. J. **35**:25, 1896.

bladder and its ducts by inflammatory adhesions. Its capacity was about 100 cc. No connection could be demonstrated between it and a cavity above or with the gallbladder and its ducts. The calcareous lining of all three cavities was bile-stained. In the omentum and mesentery there were ten or twelve nodules varying in size from that of a pea to that of a walnut, and there was one cyst attached to the wall of a left inguinal hernia. Hooklets were demonstrated in them. A stone 1.5 cm. in diameter was found in the common bile duct, and a large cyst measuring 18 by 14 cm. was found in the right kidney. It contained many daughter cysts, scolices and hooklets; however, no hooklets or scolices were found in the cavities in the lung or below the diaphragm.

Summary.—A German, aged 53, had a bronchobiliary fistula. There were multiple hydatid cysts in the omentum, mesentery and kidney. Discovery of scolices and hooklets proved them to be hydatid cysts. There was no direct proof that the cavities in the liver, subphrenic space and the right lower lobe of the lung resulted from hydatid cysts. It seems probable that the cavity in the lower lobe of the right lung was a secondary focus from rupture of the subphrenic cavity through the diaphragm.

BECK'S CASE [69] (1898).—An Austrian, aged 38, had been in the United States seven years. About six years before he had an attack of pleurisy with effusion. Serous fluid was aspirated from his chest. After slight improvement lasting about nine months, he was again taken sick. This time he coughed violently and expectorated much blood. He was then treated for consumption and admitted to a home for consumptives. About two years ago a slight swelling appeared under the angle of the right scapula, and in the course of about four weeks it became slightly painful. An incision revealed seropus and some improvement followed, but the cough accompanied by vomiting persisted as before. At last the expectoration became fetid, and the house physician, while searching for tubercle bacilli, detected hooklets and fragments of a cyst wall. A diagnosis of gangrene of the right lung was made, caused by invasion with the echinococci, and the patient was transferred to St. Mark's Hospital for operation. He was first seen by Dr. Beck on Nov. 22, 1897. Examination revealed a tall, emaciated man with a flat thorax which expanded symmetrically. The left lung was normal, but on the right side, anteriorly and below, there were tympanitic sounds and also râles during inspiration. Posteriorly and below, there was slight dulness. Correspondingly, bronchial breathing and râles were heard. The heart was normal. The pulse rate was 106, the temperature 100.5 F. The patient suffered intensely under vehement coughing spells, especially in the morning, which were always followed by expectoration of a most offensive odor. Sometimes there was dyspnea and also hemoptysis. The sputum amounted to about 200 cc. in twenty-four hours and contained an abundance of pus, also fibers of the characteristic alveolar type, pigment, hematoidin crystals, disintegrated blood corpuscles, phosphate crystals, streptococci and leptothrix. No tubercle bacilli, hooklets or cyst fragments were found. When the patient expectorated little, the dulness was not pronounced, and the respiratory sounds were less audible than in the morning after copious expectoration. On November 24, pneumotomy was performed, chloroform anesthesia being used. An incision reaching from the midaxillary line to the transverse process of the sixth dorsal vertebra was made. The fifth, sixth and seventh ribs were resected. After a portion of the soft tissues, also the costal pleura, was removed, the lung

69. Beck, Carl: Echinococcus of the Lungs, J. A. M. A. **31**:1238 (Nov. 19) 1898.

collapsed slightly but soon assumed its former expansion. The edges of the cavity being well protected with sterile gauze, a strong aspirating needle was pushed forward into the center of the exposed area which yielded only blood. After various attempts in this direction were made in vain, the stilet tip of the Paquelin cautery was introduced carefully into the center of the exposed area. After a little over 1 inch of the lung tissue had been perforated, a stream of rust-colored pus of a most offensive odor escaped with a loud noise, and at the same time the patient collapsed. A sponge was quickly forced into the opening, and under artificial respiration and energetic stimulation, the patient rallied. On the following day the cavity was carefully washed, and much pus and detritus were discharged. The drainage was copious during the next four weeks, but repeated microscopic examinations revealed nothing extraordinary. During the first week after operation, the temperature varied between 99 and 101 F., while the pulse ranged from 90 to 100. The patient slept but little, and was tortured by coughing spells. As it seemed that there was some retention, probably due to the irregularity of the draining canal, Dr. Beck introduced a finger into the cavity, dilating it thoroughly. There was a discharge of a large amount of bloody pus, and by violent coughing, a thick membrane, rolled together like a cigaret, was expelled. This proved to be a piece of a cyst wall. The patient now improved steadily, and the discharge lost its odor and became much less. The tube was discarded on February 6, and the wound was healed on February 21. He was discharged cured on July 20, 1898.

Summary.—An Austrian, aged 38, had an attack of pleurisy six years before admission to the hospital, with cough and hemoptysis. He was treated for tuberculosis. Hooklets were discovered in the sputum. Suppuration of the cyst ensued. Recovery followed pneumotomy and removal of the wall of the cyst.

CHOWN'S CASE [70] (1901).—A man, aged 56, an Icelander, had lived in Winnipeg and Manitoba. There was a long period of expectoration, and collapsed daughter cysts were expectorated for months.

Summary.—The report of this case is not available in the literature except in this brief form in Lyon's report.

GAY'S CASE [71] (1901).—Angelo, T., a barber, aged 25, born in Italy, had been in America four years. He was first seen on Jan. 10, 1901. He was always ailing up to his fourteenth year, with coughing, fever and general weakness. He was then fairly well until he was 23, when he was operated on in the Boston City Hospital for "dropsy." The scar showed that he had had a median laparotomy. He gave a history of slight attacks of hemoptysis and more or less pain constantly in the dorsal region. About Dec. 1, 1900, he became quite ill, had much cough with blood-streaked expectoration, was weak, and had anorexia, marked debility, chills and fever, and pain in the lower right side of the chest. Physical examination showed much prostration, and moderate emaciation. There was a dusky pallor of the face. The temperature was 100.8 F., the pulse rate 98 and respiratory rate 30. There were diminished respiration and crepitant and subcrepitant râles with slight dulness at the base of the right lung. Small mucous râles and crackling were present at both apexes. There was sinking in of the supraclavicular spaces. The patient apparently then had pneumonia of the right lower lobe, but recovered

70. Chown, H. H.: Case Report, personal communication of Lyon's from Chown, 1901.

71. Gay, W. F.: Echinococcus of Liver with Perforation Into the Lungs and Bronchi, Boston M & S. J. **144**:492, 1901.

by the end of January, 1901, so as to be up and about. The lower part of the right lung cleared leaving the other portions as before. At this time the liver was found to be painful and gradually enlarging. On March 1, he had several attacks of hemoptysis with much cough. Hemorrhage ceased in a few days, and and the sputum became viscid and white. The lung showed a multiplicity of râles of all kinds. He was thought to have pulmonary tuberculosis. The liver showed uniform enlargement. Abdominal tympanites was present. He had fever, and much pain on coughing. The feces were clay-colored, fetid and pasty. There was no jaundice. There was a peculiar pallor which could be called dusky. He had an anxious expression, with pinched features and cold sweats. The symptoms continued for about one week, and on March 13 had reached the maximum. On March 14, he had several vomiting spells, the matter ejected being bright yellow, suggesting bile. The expectoration became more copious and a bright orange, and in a few days the temperature declined to 99 F. The breathing became less labored. The liver was soft and decreasing in size, and the general condition slowly improved. A diagnosis of perforation from the liver into the lungs and bronchial tube was made, but the underlying pathologic process was not understood until a small fragment of white hyaline material was found in the sputum suggesting hydatid. A search of the sputum daily soon revealed an entire cyst about the size of a pigeon's egg. The expectoration of cysts then became more common and from one to ten a day, ranging in size from that of a pea to that of a pigeon's egg, were expectorated. The material was examined by Dr. F. B. Mallory, pathologist at the Boston City Hospital, who found the characteristic laminated membrane, daughter cysts and scolices. The orange color was due to crystals of hematoidin. On April 10, the patient was said to be improving; the expectoration and dark orange color had disappeared. The temperature remained 99 F. and pulse rate from 110 to 120. "This strain on the heart together with the general phthisical consolidation of the lungs will probably prove the fatal factors in the case."

Summary.—An Italian, aged 35, had been in America four years. The case was reported by the author as one of "echinococcus of liver with perforation into the lungs and bronchi." A study of this case report suggests multiple infestations involving the lungs and the liver.

STONE'S CASE [72] (1903).—An Armenian who had been in the United States seven years, for ten weeks had had progressive loss of strength and weight. He suffered with pain in the epigastrium. After two weeks of suffering he had to stop work. There was fever, but no chills. For three weeks epigastic pain was very severe, and weakness and emaciation progressed rapidly. He was much emaciated and pale, and was sweating profusely. The sclerae showed a very slight yellow tinge. There was no leukocytosis. There was some bile in the urine. The heart was normal except for weak sounds. The left lung was normal. The lower right side of the chest was bulging. There was flatness from the fourth rib in front to four fingerbreadths below the costal margin. Below the fourth interspace in front and the midscapular line in the back, there was absence of fremitus and respiratory murmur. Below the ribs, extending nearly to the midline, was a convex bulging tumor. On respiration, there was a palpable crepitus and a loud friction rub over the outer part of the tumor. There was doubtful fluctuation over the tumor. The right side of the back showed dulness at 2 inches

72. Stone, A. K.: Echinococcus Cyst of the Liver and Lungs, Boston M. & S. J. **149**:263, 1903.

below the angle of the scapula, quickly becoming flat. Respiration and fremitus were diminished and lost below the angle of the scapula. Above the dulness, respiration was harsh but of diminished intensity.

Operation was performed by Dr. C. B. Porter. An incision was made parallel to the costal margin over the tumor. At a depth of 2 inches in the liver a cyst was found containing about 4 parts of purulent material. There were many daughter cysts, varying in size from that of a pea to 2 inches in diameter. The cavity was packed with gauze because of hemorrhage. The patient died rather suddenly on the fourth day.

Autopsy on Dec. 13, 1902, showed the liver to be about normal in size. In the right lobe there was a large irregular cavity, probably 15 cm. in diameter, with a rough, irregular lining composed chiefly of a patchy layer, from 2 to 3 mm. thick, of a dirty greenish-gray, somewhat friable granular material. Adherent to this in places were plaques and patches of dense but friable dirty, grayish,

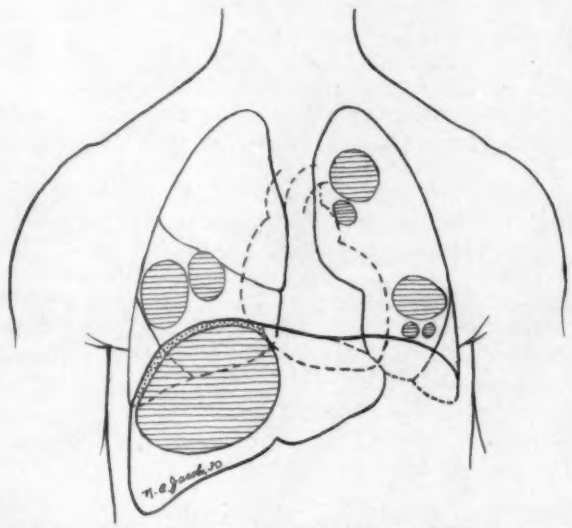

Fig. 15 (Stone's case).—Multiple cysts in both lungs and the liver.

opaque, tough substance from 2 to 3 mm. thick and not easily removed from the lining of the cavity. In places the lining resembled mucous membrane of the gall ducts, and these areas are apparently continuous with the hepatic ducts. The diaphragm was adherent to the liver and formed probably a part of the wall of the cavity. The lining of the cavity seemed to be separated from the liver substance by a thin layer of connective tissue.

In each lung, cystic structures were found in the midst of the pulmonary tissue, which bulged outwardly beneath the pleura. Where they bulged the most, they had a grayish, translucent wall apparently formed by little more than the pleura. In the median lobe of the right lung, there was a cystic structure 3 cm. in diameter. In the lower lobe of this lung there was a cyst 7 cm. in diameter. The upper lobe of the left lung contained a cyst 4.5 cm., and near this there was a collapsed cystic structure 3 cm. in diameter. The lower lobe of the left lung showed a multilocular cystic structure 6 cm in diameter and also two cysts 1.5 and 1 cm. in diameter. These were filled with a clear fluid, and possessed a

white gelatinous lining 1 mm. thick. This was readily removable, leaving a smooth surface apparently formed by a mass of connective tissue. Sections of the wall of the cysts in the left lung showed a chitinous layer with brood capsules containing scolices.

Summary.—An Armenian, who had been in the United States seven years, presented no pulmonary symptoms. He was operated on for a large cyst of the liver and died on the fourth day after operation. Seven pulmonary cysts scattered throughout the lungs except the right upper lobe were found at autopsy. Scolices were found upon microscopic examination (fig. 15).

GURLEE'S CASE [22] (1905).—Lizzie P., aged 27, a native of Italy, came to the United States in 1904. She was admitted to the Cook County Hospital on April 2, 1905. She had a cough for four months, pain in the chest and abundant expectoration, which at times had been bloody. She had had nausea and vomiting and had lost 40 pounds (18.1 Kg.).

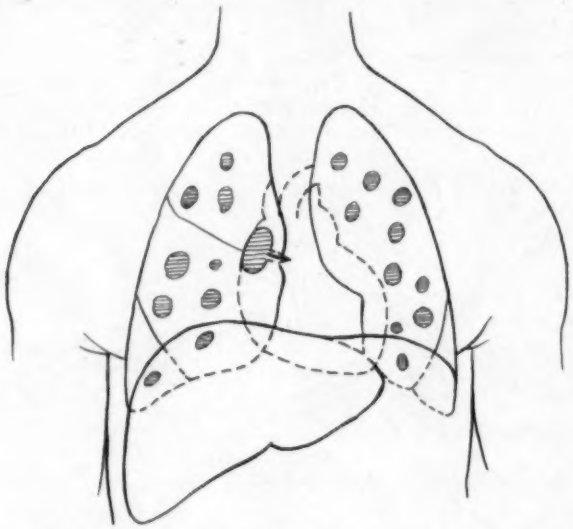

Fig. 16 (Gurlee's case).—Cyst of the right auricle rupturing into the blood stream with secondary sowing of each lung.

Examination revealed an emaciated woman who could not speak above a whisper. There was dulness from the right border of the sternum to three-fourths inch beyond the left nipple. There was a long, loud, rough, systolic murmur at the apex and a loud systolic murmur over the pulmonic area.

Dulness existed anteriorly and posteriorly over the upper lobe of the right lung, and there was some dulness posteriorly over the upper lobe of the left lung. Low down posteriorly just to the right of the vertebral column there was an area about the size of the palm with somewhat tympanitic percussion. Moist râles and bronchial breathing were heard over the right upper lobe and a few mucous râles over the middle lobe. There was bronchial breathing over the apex of the left lung with a few moist râles in the left axilla. A diagnosis of pulmonary tuberculosis was made and confirmed by examination of the sputum. The cough was violent, and there was a large quantity of purulent sputum. There was

extreme dyspnea. On April 5, she coughed up a small cyst about 1 cm. in diameter which was unruptured and showed what seemed to be a subcyst. The fluid of this cyst failed to show any hooklets, but a large number of small, round bodies found within which the echinococcus embryo was seen. The walls of the cysts were laminated. Several examinations of the sputum were negative for hooklets. The blood showed no eosinophilia. The patient died suddenly on April 10.

Postmortem examination showed no fluid in the pleural cavities. The apex of the right lung was adherent to the thoracic wall. Throughout both lungs could be palpated rounded masses, some nearly as large as a hen's egg. The left lung crepitated through, but the right upper lobe was almost solid, and in the middle and lower lobes could be felt hard, shotlike bodies, irregular in outline. On section, the left lung showed several large cysts throughout both lobes, varying in size from that of a pea to that of hen's egg. The right lung showed practically the same distribution of echinococcus cysts; the number may have been slightly greater. Disseminated tuberculosis was found in the middle and lower lobes of the right lung. A large cyst in the upper portion of the right lower lobe was removed without rupturing. The fluid contained many proligerous vesicles in which the characteristic echinococcus embryo could be seen. The wall had the characteristic laminated appearance and on its inner surface were seen numerous daughter cysts. Some of the cysts in the right lung were infected. The central portions of the lungs were nearly free from cysts. The cysts occurred mostly at the periphery of the lung.

A cyst about the size of a pigeon's egg was found in the posterior wall of the right auricle. It had ruptured internally, and a blood clot adhered to the endocardial opening. When this clot was removed, several daughter cysts varying in size from that of a pinhead to that of a pea escaped. The muscles of the heart had undergone no appreciable change, and there was a thin layer of fibrous tissue between it and the cyst. There were no cysts in other organs. Dr. Gurlee concluded that this case represented a primary cyst of the heart with secondary infection of the lungs.

Summary.—A woman, aged 27, a native of Italy, who had been in the United States about one year, had multiple cysts throughout both lungs, probably originating from a cyst in the right auricle which had ruptured into the blood stream (fig. 16).

SENN'S CASE[73] (1905).—A man, born in Greece, came to the United States about five years before examination. Six years previously he complained of acute sharp pain, which he referred to the left side and upper segment of the lung. Since then he had had occasional difficulty in breathing and attacks of coughing. His general condition on admission was fair. There was a distinct, well defined diffuse area of dulness over the left side and the upper part of the lung. The breath sounds were feeble on the left side, with bronchial breathing in the area of dulness. Aspiration was attempted in the center of the dull area, with negative results. On the night of the day on which aspiration was performed, the patient had a violent attack of coughing and raised 1½ pints or 1 quart of fluid. On microscopic examination, echinococcus hooklets and scolices were found. The rupture of the cyst was followed by a violent reaction, from which he gradually recovered. Expectoration became less and less, and instead of dulness there was resonance on percussion. A number of days after the spontaneous rupture of the cyst there was vesicular breathing.

73. Senn, Nicholas: Echinococcus Cyst of Lung, Ann. Surg. **42**:302, 1905.

Summary.—A man, a native of Greece, with symptoms of six years' duration, had pain, cough and difficulty in breathing. There was spontaneous rupture of the cyst in the left lung into the bronchial tree following a negative aspiration. Hooklets and scolices were found in the sputum.

GARRETT'S CASE[74] (1906).—L. S., a colored woman, aged 46, a native of Worcester County, Maryland, was admitted to the State Asylum on Feb. 19, 1889, for treatment for manic-depressive psychosis. Her general health was excellent for twelve years, when attacks of syncope developed which were followed by more or less stupor lasting several days. These attacks were evidently nephritic, as the urine contained hyaline and granular casts in abundance. There was marked arteriosclerosis. She soon improved, and remained in fairly good health until the final illness. On April 16, 1906, after a few days of apparent malaise and indisposition, she began to have a mild diarrhea accompanied by nausea, vomiting and slight fever. On May 2, she had "a chill followed by fever of 104 F." At this time cough was first noted.

Physical examination revealed dulness over a limited area of the right middle lobe, posteriorly, with coarse râles. A septic temperature persisted. There was rapid loss of weight. The sputum was swallowed, and only once could it be examined. No tubercle bacilli were found, but elastic tissue were present. She died on May 27, of what was thought to be pulmonary tuberculosis.

Autopsy showed a cavity the size of a hen's egg in the upper portion of the middle lobe of the right lung, posteriorly. It was surrounded by a thick wall, and contained dark brown fluid not unlike thin, dirty pus. The cavity communicated with a bronchus. The cyst containcd the same layers as described in the cyst of the liver. In the center of the right lobe of the liver there was a cyst about the size of a fist. It contained yellowish, granular, semisolid, caseous material resembling curd. The walls of the cyst were thick, sharply defined and easily separated into two distinct layers, the inner one being thicker, grayish and friable. The outer layer was thinner, darker and much tougher. Hooklets were found in each cyst. No scolices were demonstrated.

Summary.—A woman, aged 46, native born, an inmate of the state asylum for about seventeen years, had a hydatid cyst of the right middle lobe which ruptured into a bronchus. It was infected. A quiescent cyst was found in the liver. The diagnosis was made at autopsy. Hooklets were found.

SMITH AND HARRINGTON'S CASE[75] (1907).—Alexander Auchals, aged 23, was born, and had always lived, in southern Russia. About six weeks before entrance to the hospital, on Dec. 12, 1906, he had left home and sailed for America. At that time he felt well. On the ninth day of his journey, he began to have pain in the right side of the chest, which had been fairly constant since them. The pain had no relation to deep breathing, cough, position or food. There was no cough or sputum. On admission to the hospital, the whole right side of the chest was flat throughout. The heart was 1¼ inches outside the left nipple line. The liver dulness was 2 inches below the costal margin. The interspaces in the right side of the chest were noticeably obliterated. There was bronchial breathing with a suggestion of amphoric note with bronchophony over the right side of the chest. Aspiration was performed on this side just below the angle of the scapula, with

74. Garrett, R. E.: Hydatid Cysts with a Report of a Case, Maryland M. J. **49**:373, 1906.

75. Smith, W. H., and Harrington, F. B.: A Case of Echinococcus Cyst of Lung and Abdomen, Boston M. & S. J. **156**:180, 1907.

negative results. Aspiration was again performed in the posterior axillary line, where there was absolute flatness, and thin, turbid, greenish fluid was obtained which did not flow readily. A little more than 1 pint was withdrawn. There were no bacteria in the sediment, which was composed of pus cells. No hooklets were found, but subsequently after protracted search they were demonstrated. Subsequently he was tapped twice in the posterior axillary line, and 1 pint of similar fluid was withdrawn each time. The patient did not do well. He had some pain in his side, and there was a rise in temperature to 101 F. Operation was performed on December 19. A portion of the eighth rib was removed, and the pleural cavity opened. There was a flow of several pints of fluid containing cysts in large numbers. A short time afterward cysts were found filling the pelvis and pressing on the bladder.

Summary.—A man, aged 23, born in southern Russia, was sick on arrival in the United States. The chief symptom was pain in the right side of the chest. There was no cough or expectoration. There were physical signs of fluid in the right pleural cavity. Turbid green fluid was aspirated from the right side of the chest on three occasions. Thoracotomy was performed by removal of a section of the eighth rib. Several pints of fluid containing a large number of cysts was evacuated. Hooklets were found in the pleural fluid. This case is recorded in the literature as a "case of echinococcus cyst of the lung and abdomen;" it is more likely a case of pleural cyst.

MacDonald's Case[76] (1913).—A youth, aged 18, a native of New Zealand, was admitted to St. Joseph's Hospital, San Francisco, on May 22, 1912, complaining of cough, weakness and shortness of breath and expectoration of pus and pain in the left side of the thorax for a time. Two and a half years before admission, he had lived in one of the notorious hydatid areas in New Zealand.

Examination revealed the apex of the heart about 1½ inches to the right of the sternum. The left side of the thorax gave a complete typical picture of hydropneumothorax. Operation was performed on May 5, 1912, with the patient under ether anesthesia. Resection of 2 inches of the seventh, eighth and ninth ribs in the midaxillary line was done. A considerable amount of semipurulent fluid and a large number of collapsed and dead hydatid cysts together with two large normal ones were obtained. The total amount of fluid and cysts measured 3 quarts. A second operation was performed on June 10, when a portion of the tenth rib close to the spine was resected to give better drainage. There was a bronchopleural fistula. He was discharged on September 17. He still had two drainage tubes in the pleural cavity which held about 3 ounces and communicated with a bronchus. He was last heard from by letter on November 17, when he reported that he was much improved, and that his back was nearly healed.

Summary.—A youth, aged 18, a native of New Zealand, had a cough, purulent expectoration, and pain in the side. The picture was that of hydropneumothorax. Three quarts of purulent fluid and hydatid cysts was obtained from the left side of the chest by thoracotomy. The patient was well on his way to recovery when last heard from. This case probably represents a pulmonary hydatid cyst rupturing into the pleura and into a bronchus, such as has been described by Deve.

Ramey and Emerson's Case[77] (1915).—A Greek, age not given, about one month before coming under observation had been in a hospital for one week

76. MacDonald, G. C.: Hydatid Cyst of Left Lung, Pacific M. J. **56**:271, 1913.

77. Ramey and Emerson: Echinococcus Disease: Report of a Case, West. M. Rev. **20**:171, 1915.

and had been treated for pneumonia. Following this he coughed a great deal and did not regain strength. The history was unsatisfactory, because he could not speak English. Physical examination revealed absolute dulness over the lower posterior area of the right side of the chest. The breath sounds were absent. A soft, tense tumor, transmitting a peculiar thrill on percussion, was present in the right epigastric region, apparently closely associated with the liver. The palpable portion of the tumor was as large as an orange. Frequent examinations of the sputum were negative for hydatid elements. Exploratory aspiration of the chest revealed a spurt of reddish-yellow fluid, then sudden complete stoppage of the flow. Examination of this fluid did not show hooklets or other evidence of echinococcus disease. The patient rapidly became emaciated, and had an irregular temperature. Operation consisted of the resection of three ribs. There escaped from the wound about 2 quarts of yellow pus tinged with red and about 200 cysts of all sizes, from that of a pinhead to that of an orange. All of the cysts were brown, collapsed and dead. In the subsequent drainage, other cysts appeared from time to time. About one month later, a large cyst of the liver was treated by operation. Drainage from the wound in the chest persisted for several months. It finally healed, but after a period of two or three months broke open and discharged. He then had a cough, lost flesh and expectorated two or three collapsed brown cysts. The patient disappeared from observation. Scolices and hooklets were recovered in the fluid from the cyst of the liver.

Summary.—A Greek, age not known, had a cough. A cyst with daughter cyst formation was found in the right pleural cavity, probably originating in the lung. It was complicated by a hydatid cyst of the liver. He was improved by operation, but disappeared from observation while drainage still persisted from the right side of the chest.

Davis and Balboni's Case [78] (1917).—A man, aged 27, an Italian fruit pedler, had been in this country fifteen years. He was admitted to the Massachusetts General Hospital on Aug. 23, 1912 (service of R. I. Lee). In 1910, he had had a severe attack of pain in the epigastric region. At this time he first noticed a small swelling below the ensiform appendix. Similar attacks at irregular intervals had persisted. After two years the swelling had increased perceptibly. Examination revealed just below the ensiform appendix a prominence which moved with the liver on respiration. It was smooth, doughy and tender. The mass apparently sprang from the left side of the liver. The right side of the chest was dull from the inferior angle of the scapula down, and an occasional dry crackle was heard. Roentgen examination gave negative results. The Wassermann reaction was negative. The white blood count was 5,200, eosinophils 1 per cent and hemoglobin 80 per cent. The coagulation time was seven minutes. A diagnosis of echinococcus disease of the liver was made and operation suggested. The patient refused to remain in the hospital longer than one week. On Jan. 22, 1915, he was operated on by Dr. R. P. Bonnelli in a private hospital. A huge cyst of the liver was removed at operation. Scolices were found. On January 26 and February 10, the echinococcus-fixation test gave strongly positive results. He was discharged in good condition on February 13. The sinus on the right seemed to communicate with the chest cavity, for when the patient coughed there was an expulsion of air through the sinus. During the rest of February and March the patient had a dry cough and evening fever. The sputum was negative for tubercle bacilli.

78. Davis, L., and Balboni, G. M.: A Study of Twenty-Nine Cases of Echinococcus Disease, Boston M. & S. J. **176**:826, 1917.

Examination showed consolidation of the medial and inferior lobes. He expectorated large quantities of mucus, sometimes bright red and at other times of prune juice appearance. Hooklets were present in the sputum. The cough and expectoration decreased and disappeared in June. The sinus was completely healed in May. The echinococcus-fixation test was negative on December 7. At the time this case was reported, May 24, 1917, the patient was well and working.

Summary.—A man, aged 27, an Italian had been in this country fifteen years. A hydatid cyst of the liver was cured by operation. It was complicated by a hydatid cyst in the right lung, which apparently cured itself by drainage into the bronchial tree. Hooklets were found in the sputum.

CLARKSON'S CASE [79] (1917).—A Macedonian youth, aged 18, was admitted to the hospital on April 14, 1912, complaining of pain, cough and shortness of breath, which began with a chill two weeks prior to admission. Respiration was 46, temperature 101 F. and pulse rate 100. In the left lung there was a rounded and circumscribed area of dulness extending from the second to the sixth rib and from the mammillary line in front to the inferior angle of the scapula behind. The breath sounds were distant and the vocal resonance much diminished in this locality. The rounded area of dulness and the shape of the shadow on the roentgenogram suggested a cyst. On aspiration, 510 cc. of clear, limpid fluid was obtained which on examination showed slight traces of albumin and many heads and hooklets of the echinococcus. The white blood cells numbered 23,000 with no increase in the eosinophils. Operation was performed, and a large cyst of about 12 ounce capacity was rather easily removed. It contained many daughter cysts. The recovery was slow and tedious, a sinus persisting for a long time.

Summary.—A Macedonian youth, aged 18, suffered from pain, cough and shortness of breath. The diagnosis was made by an exploratory aspiration. The cyst was removed at operation, and recovery slowly followed.

CLARKSON'S CASE 2 [79] (1917).—An Italian, aged 25, a laborer, was admitted to the Toronto General Hospital on June 15, 1914, complaining of severe pain on the left side, which was increased on coughing. The onset was sudden accompanied by a chill. The temperature was 102 F. and respiratory rate 30; the sputum was bloody. The left side of the chest was decidedly limited in its movements. Posteriorly, there was an area of absolute dulness above this relative dulness as high as the fifth rib. The heart was slightly displaced toward the right. Fluoroscopic examination showed the diaphragm on the left side to be 8 cm. below the nipple, immovable but arched. The costophrenic angle was clear. In the middle portion of the left lung toward the base was a large rounded shadow which did not move on respiration. On exploratory aspiration, 25 cc. of clear fluid under slight pressure was obtained. This was of low specific gravity and contained a slight trace of albumin but no hooklets. The patient's general condition improved, and he was discharged from the hospital and lost from observation until April 6, 1915, when he was admitted to the Western Hospital suffering from a troublesome cough with abundant sputum. He also had a severe pain in the left side. The temperature was 102.4 F., pulse rate 100 and the respiratory rate 28. The left side of the chest showed restricted movements, and vocal fremitus was absent over the lower quadrant. There was absolute dulness below the seventh rib anteriorly. Posteriorly, beginning at the level of the seventh dorsal spine, there was relative dulness. In the lower part of the chest there was absolute flatness. Over the dull area, the breath sounds were absent. Exploratory puncture in the ninth space,

79. Clarkson, F. A.: Hydatid of Lung, Canad. Pract. & Rev. **42**:139, 1917.

posterior axillary line, yielded 1 cc. of fecal-smelling pus in which staphylococci and bacilli were found. The white blood cells numbered 9,000, with few eosinophils. Operation was performed on May 6. A portion of the ninth rib was resected in the posterior axillary line. At some distance from the surface was found a cyst full of foul-smelling pus, the walls of which were thin and gelatinous in structure and came away by piecemeal. No daughter cysts were obtained. The patient tolerated the operation poorly. He coughed up large quantities of the cyst wall and quantities of blood. After a rather slow convalescence, he made a good recovery.

Summary.—An Italian, aged 25, a laborer, presented the symptoms of pain in the left side, cough and hemoptysis. The onset was acute. The diagnosis was made by roentgen examination and aspiration on the first admission to the hospital, but he was discharged and disappeared from observation for nearly a year, when he returned with a suppurating cyst which was cured by operation.

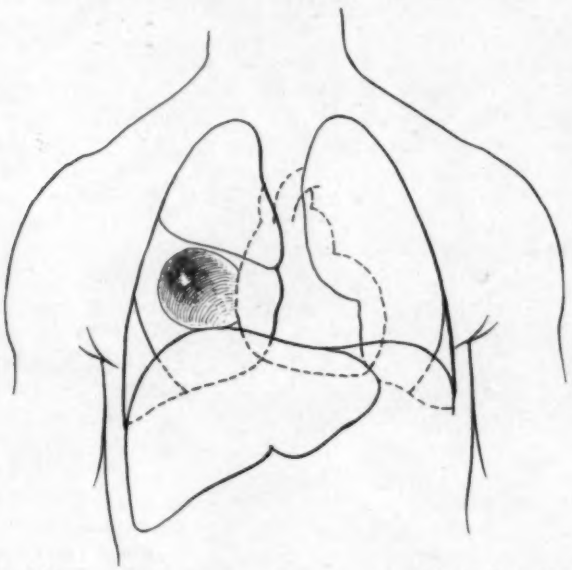

Fig. 17 (Crow's case).—Large solitary cyst in the right middle lobe.

Crow's Case [80] (1918).—A farmer, aged 30, a native of Spain, was first seen in November, 1917. His present trouble began five years before admission, with intermittent pains in the upper part of the back. Six months later he began having gastric distress and indigestion. The results of the physical examination were negative. The patient was referred to the x-ray laboratory for examination of the gastro-intestinal tract. A roentgenogram revealed a cyst in the lower right side of the chest, 12 by 10 cm. Operation was performed on November 18, with the patient under nitrous oxide anesthesia. A trap door incision was made in the anterior right side of the chest over the third, fourth and fifth ribs. When the pleura was opened, the lung was collapsed, and embedded in its tissue was seen the white, glistening, mother-of-pearl-like surface of the cyst. The cyst was attached to the pericardium and pleura. The inner layer of the cyst was dissected away

80. Crow, L. B.: Echinococcus Disease of the Lungs, Am. J. Roentgenol. 5: 513, 1918.

from the outer fibrous layer and, when freed, lifted through the opening, where it unfortunately burst and allowed the contents to spill in the chest cavity. The cavity was well sponged. An attempt was made to remove some of the outer fibrous layer, but the slightest traction on the lung caused immediate cessation of respiration, so that this attempt was given up. The cavity was packed with gauze, dipped in 10 per cent formaldehyde glycerin solution. The wound was closed. The immediate postoperative convalescence was very stormy. After a few days, the lung began to expand. For two weeks, the patient had a septic temperature. Three days after operation he had a profuse expectoration of brownish mucopurulent pus, accompanied by severe attacks of coughing. He gradually improved, so that at the time of this case report he had recovered and was soon to leave the hospital as cured.

Summary.—A Spaniard, aged 30, presented no pulmonary symptoms other than pain in the back of five years' duration. The diagnosis was made from roentgen examination; cure was apparently obtained by pneumotomy. No report of the microscopic examination was given (fig. 17).

GLASSMAN'S CASE [81] (1922).—A woman, aged 30, a Siberian, was admitted to the hospital on Jan. 6, 1922. For eight months she had had belching, nausea and vomiting after meals. A dull more or less continuous pain later developed in the right side of the abdomen. There was a mass in the right hypochondriac region, which was smooth and tender. It moved with respiration. The clinical diagnosis was hydrops of the gallbladder. Roentgen examination showed a mass in the right hypochondriac region, and the roentgen diagnosis was cyst of the liver. Operation was performed on January 17, when three cysts of the liver were found. The largest was about the size of a grapefruit. Two cysts were removed; one was packed with gauze. The patient died on January 18. Postmortem examination revealed two cysts in the right lower lobe of the lung and one cyst in the left upper lobe. The cysts occupied about two thirds of the lung. There were no pulmonary symptoms, and no roentgen examination of the chest had been made.

Summary.—A Siberian woman, aged 30, died following operation for multiple cysts of the liver. At autopsy, two cysts were found in the right lower lobe and one cyst in the left upper lobe.

BALBONI'S CASE [43] (1922).—A. A., aged 22, a Greek, a farm hand, had been in the United States five years. He was admitted to the outpatient department of the Massachusetts General Hospital on Feb. 17, 1917. His chief complaints were cough, pain in the chest and blood in the sputum. He had had a cough for two years. One and a half years before admission, after slight exertion, he coughed up a teaspoonful of bright red blood. About one year before he coughed up one glassful of bright red blood. He remained in bed for three months, and had bloody sputum daily in streaks and clots. He then resumed work, but every three or four weeks had a little bloody sputum. One month before examination he coughed up one teaspoonful of blood. During the past one and a half years the cough had been slight, mostly in the morning. He raised two or three teaspoonfuls of sputum during the course of the day. He felt well and was able to work without feeling tired. He had a good appetite, but had lost some weight. He had had no night sweats. Three or four days before admission he felt tired and was unable to work. He had a true chill late the next evening and felt feverish. He also had some pain in the anterior right side of the chest on coughing.

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81. Glassman, J.: Radiological Findings in a Case of Echinococcus Cyst of the Lung and the Liver, M. J. & Rec. **119**:144, 1924.

The chest was well developed, and expansion was equal. There was dulness at the base of the right lung posteriorly and anteriorly, with diminished breath sounds and whispered voice from about one fingerbreadth from the angle of the scapula downward. The abdomen was slightly tender over the liver, which was palpable. The sputum was negative. The blood smear was normal. The Wassermann reaction was negative. The echinococcus fixation was negative. Roentgen examination (by Dr. G. W. Holmes) showed a round tumor mass at the base of the right lung, about the size of a grapefruit. The lower border was mostly below the dome of the diaphragm. This shadow did not move with ordinary respiration, but could be displaced somewhat with forced respiration. It was of even density throughout, and its borders were sharply defined.

Thoracotomy was performed (by Dr. W. Whittemore). The right seventh and eighth ribs were resected below the angle of the scapula. The pleura was somewhat thick, and there were many fine adhesions between the pleura, and a firm

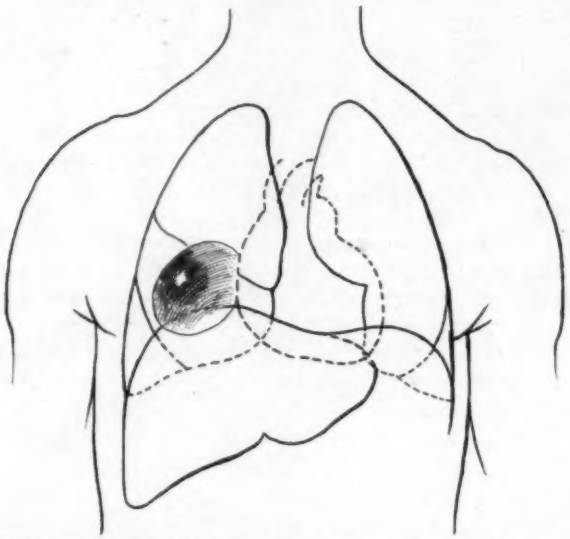

Fig. 18 (Balboni's case 1).—Large solitary cyst in the right lower lobe.

mass in the right lower lobe. The mass was sutured to the pleura, and an incision about 1 inch deep into the mass seemed to go through lung tissue. A needle was inserted ¼ inch further, and a small amount of clear fluid found. The patient began to expectorate clear fluid through the nose and the mouth. Finger dissection into the mass opened a large cyst filled with clear fluid. About 1,500 cc. of clear fluid was evacuated. No small cysts or hooklets were found. A cigaret drain was introduced into the cavity.

According to the pathologic report, there was chronic inflammation, but no evidence of echinococcus. The patient was discharged on Jan. 6, 1918. The wound was clean and solidly healed. He was readmitted to the hospital on Sept. 19, 1919, and gave the following history: Since leaving the hospital he had had a persistent cough, especially in the early morning and at night. He had still raised a small amount of blood, sometimes bright but usually dark. He had had no large hemorrhage. There had been dull pain in the lower right side of the chest. He had been working on a farm up to ten months previously, when the pain became too severe for him to continue work. He had not lost weight, but felt weak.

Examination of the thorax showed some limitation of motion of the base of the right lung. There was dulness from the seventh rib down on the right side of the back, extending in the front to the fifth rib. There were absent tactile fremitus, diminished to absent whispered voice, vocal fremitus and breath sounds in the area of impaired resonance. On September 24, with the patient under gas-oxygen anesthesia, thoracotomy was performed by rib resection (Dr. Whittemore). The lung was adherent to the costal pleura. A large tumor mass presented in the lung. On opening into this, it proved to be a large cyst, and a considerable amount of clear fluid was evacuated. Several large fragments of cyst wall were removed. The cavity was packed with gauze, and the wound closed. Packing was removed on the fourth day, and on the following day the remainder of the cyst was expelled through the operative wound. In three weeks the incision was healed, and the patient had an uneventful convalescence.

According to the pathologic report, irregular pieces of the wall of the cyst showed smooth, pearly white surfaces which had an elastic consistency. No hooklets could be found on fresh examination. Microscopic examination showed a laminated membrane without cellular structure. The gross and histologic appearance was in every way consistent with that of an echinococcus cyst.

Summary.—A Greek, aged 22, who had been in the United States five years, had symptoms of cough and pain in the chest and blood in the sputum of from one and one-half to two years' duration. The cyst was drained at the first operation, but the cyst wall was not removed. About twenty-one months later the cyst wall was removed at a secondary operation. Scolices or hooklets were not discovered, but the cyst wall had the characteristic appearance of a hydatid cyst (fig. 18).

BALBONI'S CASE 2[43] (1922).—P. P., a Greek, aged 25, a laborer in a cotton mill, had lived in the United States for five years. He was admitted to the out-patient department of the Massachusetts General Hospital on Sept. 24, 1919. His chief complaints were pain in the chest and cough with blood in the sputum. About two years before admission he was hit on the right side by a piece of iron which fell on him. He was in a hospital in Youngstown, Ohio, for four months. At this time he began to cough a great deal, often raising bloody sputum. He felt fairly well after leaving the hospital, and the cough left him. About six months later, cough and hemoptysis returned, and the pain increased in the chest. He was unable to work for seven months. He sometimes had pain in the left side of the chest also. He was well until the onset of the present illness. He was a shepherd in Greece, and had dogs associated with him.

Physical examination showed a well developed chest; there was greater expansion on the left side than on the right. The heart was normal in size and position. The right side of the chest was dull below the spine of the scapula almost to flatness with râles and bronchial breathing. It was dull in the axilla. There were râles in the lower half of the left lung with some bronchial respiration. Examination of the blood showed: white cells, 7,800; red cells, 7,396,000; hemoglobin, 100 per cent; polymorphonuclears, 78 per cent; eosinophils, 5 per cent; mass cells, 5 per cent; lymphocytes, 5.5 per cent, and large mononuclears, 11 per cent. The Wassermann reaction was negative. The reaction to the echinococcus-fixation test was strongly positive. The sputum was mucopurulent and was negative for hooklets, fragments of membrane or tubercle bacilli. Roentgen examination (by Dr. G. W. Holmes) showed an area of increased density 4 cm. in diameter in the left side of the chest below the fifth rib. It was round and of even density, with sharply defined borders. When the position of the tube was changed overlying it, there was a ringlike shadow of diminished density, which changed its relation

suggesting a different plane to the dense shadow. Neither shadow reached the periphery. A similar, slightly larger process was seen in the right lung below the fourth rib. On Feb. 16, 1920, a roentgenogram made following oxygen inflation of the abdomen showed a distinct outline of the liver and the spleen. They appeared to be normal in size and shape. Just below the lower margin of the liver there was a round, dense mass, which was apparently connected by a band of adhesions to the anterior abdominal wall. There was a ringlike shadow in the left kidney, having all the appearance of an echinicoccous cyst. The patient received nine roentgen treatments between Oct. 3, 1919, and May 15, 1920, at from two to four week intervals. There was no improvement in the symptoms or change in the roentgen observations nor any change in the fixation test taken on three different occasions. When last seen in May, 1920, he still complained of an irritative cough, occasionally blood-streaked sputum and pain in both sides of the chest and in the region of the left kidney.

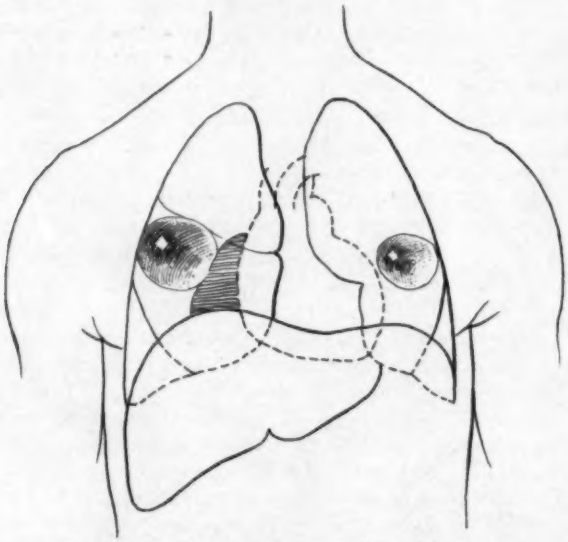

Fig. 19 (Balboni's case 2).—Bilateral cysts.

Summary.—A Greek, aged 25, a shepherd while in Greece, had been in the United States five years. The symptoms presented were pain in the chest, cough and hemoptysis. The echinococcus-complement fixation test gave strongly positive results. There was roentgen evidence of hydatid cysts in the lower part of the lungs, and in the left kidney and an intraperitoneal cyst below the liver. There was no improvement following roentgen therapy (fig. 19).

MILLS' CASE [82] (1922) (Case of Dr. A. F. Wagner).—J. G., a French woman, aged 36, was found dead. On Jan. 21, 1922, postmortem examination showed a hydatid cyst of the right ventricle of the heart, 5 cm. in diameter. It had the typical laminated cyst wall. There were no daughter cysts or scolices. In the substance on the inner side of the lower lobe of the right lung, there were four cysts the size of a walnut. The left lung was normal.

82. Mills, H. W.: Hydatid Cysts of the Heart, with Report of a Case, Surg. Gynec. Obst. **35**:455, 1922.

Pathologic examination (Dr. Brem and Dr. Zeiler) showed a rounded prominence about 4 cm. in diameter at the apex of the right ventricle. In the center of the ventricle the apical portion was narrowed by a mass lying in the apex and pushing upward and inward the surface of the intraventricular septum. Section of this mass showed an old cyst 5 by 4 cm. Attached to its wall was a crumpled, folded membrane which was more or less translucent. The cardiac tissue covering the cyst was little more than the endocardium. The left ventricle was of normal size and was not invaded by the cyst. Microscopic examination of a section from the wall of the cyst showed an eosin-staining lanceolated membrane without nuclei and outside this a fibrous connective tissue capsule. About this was a zone of inflammation containing a few round cells and great numbers of eosinophils and lymphocytes. The diagnosis was echinococcus cyst of the heart.

Summary.—A French woman, aged 36, was found dead. At autopsy a hydatid cyst was found in the right ventricle and four cysts in the lower part of the right

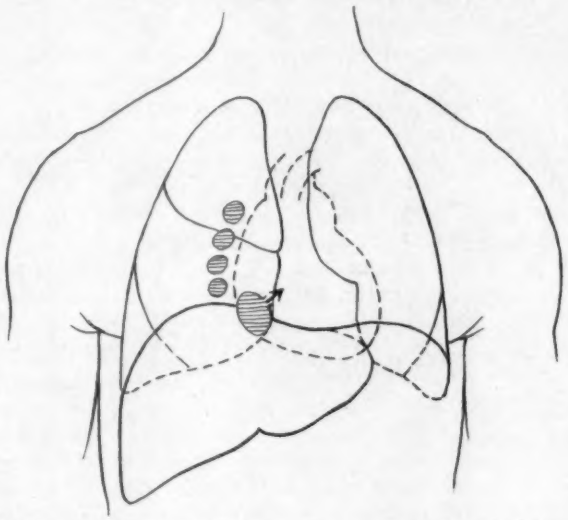

Fig. 20 (Mills' case).—Cyst in the wall of the right ventricle; multiple cysts in the right lung.

lung. Dr. Wagner believed that the process started in the lungs and infected the heart by direct extension. Dr. Mills believed that the cyst of the heart was primary and the pulmonary cysts metastatic from it. As there was no evidence that the cyst in the right ventricle had ruptured into the blood stream, it is probable that the cysts of the lung and that of the heart had no immediate connection, all being the result of a primary infestation (fig. 20).

CURRAN AND LOCKE'S CASE [55] (1924).—A Syrian woman, aged 52, was admitted to the hospital on Dec. 12, 1918. She had been in the hospital on three previous occasions, first in 1909, when she was operated on for a large cyst of the liver containing innumerable daughter cysts. The second admission was four months later because of a discharging sinus. The third admission was in 1912, during which hospitalization she was operated on for recurrence of the hydatid cyst of the liver. Physical examination at the time of the present entry showed a well developed and well nourished woman lying in bed, with great dyspnea and pain.

The chest was flat on the right side to the third rib posteriorly with absence of breath sounds. There was slight bulging of the interspaces over this area. The abdomen was greatly distended. There was a large, hard tumor on the right, extending from the costal margin to the crest of the ilium and to the navel in the midline. There was also a smaller mass hanging just below the ensiform appendix. Aspiration was performed on the right side of the chest through the eighth interspace in the midscapular line, and "a small amount of straw-colored fluid was withdrawn. The needle was passed in different directions and small cysts were apparently tapped with the withdrawal of a small amount of fluid from each one." Microscopic examination showed echinococcus remnants in the fluid. This patient died following laparotomy, at which time a large cavity containing a great quantity of purulent, foul-smelling fluid was drained.

Summary.—A Syrian woman, aged 52, had multiple recurrent hydatid cysts of the liver. She died following an operation for a secondarily infected abdominal cyst. The location of the intrathoracic cyst is not clear from the description. It may have been pleural or pulmonary.

CAMPBELL'S CASE [83] (1925).—A Russian woman, age not given, gave a history of gradually increasing thoracic distress. Examination showed well marked dulness over the lower left side of the chest with increased temperature, sweating and rapid pulse. The heart was displaced to the right. Exploratory aspiration recovered white, glairy pus. Rib resection recovered thousands of cysts varying from minute to very large. In the postoperative treatment, the patient was able to taste antiseptics used in irrigating. The cavity was slow in obliterating, and extensive resection of several ribs was done in order to decrease its size. Following the use of injections of bismuth paste, the patient made a fairly rapid recovery. She was again seen in September, 1919, with symptoms referable to the upper right portion of the abdomen. The roentgenogram showed a high diaphragm on the right side. An operation revealed a cyst below the liver, which after having been walled off with packing for nine days was enucleated at a second stage. It proved to be an echinococcus cyst.

Summary.—A Russian woman, age unknown, had a suppurating cyst in the left pleural cavity containing daughter cysts. A pleurobronchial communication existed. It is not possible to determine from a study of the record whether or not this cyst had a pulmonary origin.

MAGATH'S CASE [4] (1921).—A man, age not given, was born in the United States, but had traveled in the Philippine Islands in 1908. He lieved in Nebraska.

Summary.—No details of this case report are available, as far as I can determine. The brief summary as given appears in a table of the Mayo Clinic cases reported by Magath.

ORTENBERG'S CASE [84] (1929).—A girl, aged 12, was first seen during November, 1923. She complained of pain in the lower right part of the chest, and she had a dry cough. The temperature was 102 F.; the pulse was rapid. There was a hectic flush of the cheeks. No cyanosis or respiratory distress existed. At the base of the right lung posteriorly there was a rounded area of dulness over which the breath sounds were absent and the tactile and vocal fremitus were diminished. Ten days after the onset of the illness, during a fit of coughing, the patient nearly choked in the act of bringing up a large quantity of fluid together with what, according to the father's description, looked like a "small white, crumpled handker-

83. Campbell, C. C.: Echinococcus, Journal-Lancet **45**:572, 1925.
84. Ortenberg, S.: Case Report, Canad. M. A. J. **20**:284, 1929.

chief." The entire expectoration was retained in a tumbler and consisted of 5 or 6 ounces of a cloudy, watery fluid holding a partially suspended, gelatinous sediment. Microscopic examination showed an abundance of pus, elastic fibers and alveolar cells, but no hooklets. There was no hemoptysis. A puncture of the pleura was unproductive. Less than two years before this time, two echinococcus cysts had been enucleated from the liver. The roentgenogram of the chest three days after spontaneous evacuation of the cyst showed the presence of a dense, homogeneous shadow about the size and shape of an orange, in the outer portion of the base of the right lung. The margins of this shadow were convex and fairly definitely outlined. The patient made a rapid recovery following the vomica. Roentgen study five weeks later showed a small area of mottling in the middle portion of the lower third of the right side of the chest. A third roentgenogram taken on Dec. 5, 1928, five years later, showed a circular shadow of calcification in the base of the right lung in the ninth interspace.

Summary.—A girl, aged 12, gave the history of having had two echinococcus cysts removed from the liver. The cyst in the lower part of the right lung was expectorated and apparently cured by drainage through the bronchial tree.

ABSTRACT OF DISCUSSION

Dr. Howard Lilienthal, New York: I have had one case of hydatid cysts of the lung in a person who was born in Greece and who left there when he was very young, which brings up the point that is mentioned in the literature that people who have hydatid cysts have had them from early childhood, and that such cysts have never been proved to have developed after adult life. This may or may not be so. I should like to know what some of the other members of the society think about it. In case there is a calcification of the wall of the cyst, I think that it is a good thing to divide the operation into two parts; first, take out the contents of the cyst and later, in an aseptic field, get rid of as much of the calcified capsule as possible.

I have drawn out the wall of what must have been enormous hydatid cysts from behind the sternum of one patient, taking out one piece every day or two until all had been extracted. The patient recovered. He came to the hospital with only a small sinus and nothing to indicate what had been the cause; it was not until I began taking out what I thought to be plates of bone that the diagnosis was made. I enlarged the incision and removed larger flat fragments. The curved form of the plates was suggestive. This operation was performed long ago, and no roentgenographic study was possible.

Dr. Willy Meyer, New York: We are indebted to Dr. Phillips for bringing this interesting subject before us. Cases of hydatid cysts are comparatively rare in our country. They are frequently found abroad, for instance on the southern shore of the Baltic Sea; a great many cases have been reported from there.

I remember a case in 1882, when I was a young doctor at the Surgical Clinic of Bowen University, in which the pleural cavity was punctured because all the symptoms pointed to an empyema. A yellowish, rather turbid fluid was obtained. The patient was operated on. Much to our surprise, a great many larger and smaller cysts floated in the fluid. It was a hydatid cyst of the pleural cavity. The patient recovered.

In the middle of the nineties, I did a catheterization of the ureters in a man. The report on the obtained specimens came back from the pathologic laboratory with the emphasis that echinococcus hooks were found. In this case we had to deal with a hydatid cyst of one kidney. Unfortunately, the patient was not

operated on, but the specimen was absolutely convincing. Hydatid cysts can be found in any organ. The cases of Dr. Phillips show what one has to think of in making a diagnosis. In the presence of cysts, one should never forget the hydatid.

Dr. F. S. Johns, Richmond, Va.: I had a case of this kind in a Virginian, a senior medical student who had been abroad two years during the World War. He came back with considerable loss of weight. One of our internists, Dr. Douglas Vanderhoof, found that he had a tumor of the right lung revealed by roentgen examination. I operated on him and found a calcified cyst, about the size of an orange. After the cyst was removed I sent the specimen around to several pathologists, which resulted in an undetermined diagnosis. About one year following the operation, fortunately or unfortunately an infection developed in the patient's pleura. The diagnosis was confirmed through finding the hooklets. After excision of the involved pleura he made a complete recovery. I reported this case several years ago before the Interurban Surgical Society, but it was not published. I should be glad to have Dr. Phillips add this case to his series.

Dr. Pol N. Coryllos, New York: Dr. Phillips presented a remarkable study of the hydatids of the lungs. As I come from a country—Greece—in which hydatic cysts are a common occurrence, I wish to add only a word to that question. This is a word of warning against diagnostic tapping of these cysts. The patient is often highly sensitized by hydatic fluid, so that even a fraction of a drop entering the circulatory stream or even the subcutaneous tissue can produce severe anaphylactic shock. I will always remember a case of a young girl of 25, who nearly died after such an exploratory puncture. A second danger of these punctures, especially in the cysts of the liver, is the possibility of spreading about scolices and thus causing secondary echinococcosis, particularly in the peritoneal cavity. The same thing may occur in the pleural cavity, therefore I believe that Devè's method should always be used in these cases.

Dr. Edgar W. Phillips, New York: I think that every one agrees with what Dr. Lilienthal said about the age of infection, that is, that it occurs during childhood. Deve and Stonewell both emphasized that point.

Dr. Lilienthal spoke of the calcified pericystic layer; that is, the layer thrown out by the host surrounding the invader. When that is thick walled, the majority of surgeons drain the cyst cavity. In the lung, this pericystic layer is usually thin, and the lung cavity surrounding the hydatid cyst very rapidly obliterates so that they have been drained for a very short time in countries in which the disease is common.

Dr. Meyer emphasizes the rarity of hydatid cyst in this country. I do not know how long the cases are going to be rare if certain reports are true that in some instances 100 per cent of hogs slaughtered are found to have hydatid disease. We have reports from Virginia, where 100 per cent has been found, and scattered all over this country are reports of high percentages of infestation, particularly in hogs.

The chief of the Zoological Department, Bureau of Animal Industry, says that there is no way at present of knowing how much infestation there is in this country.

Dr. Coryllos spoke of the danger of anaphylaxis from aspiration. All of the reports I read on this subject condemned aspiration either for treatment or for diagnosis, both because of anaphylaxis and because of the danger of secondary sowing.

GIANT SARCOMA OF THE PLEURA

REPORT OF TWO CASES WITH REMARKS ON OPERATIVE EXPLORATION OF THE THORAX

HOWARD LILIENTHAL, M.D.
NEW YORK

CASE 1.[1]—*History.*—Mrs. I., aged 48, came to see me in December, 1929. Her family history was unimportant. About twenty years before, she had had the last of two miscarriages, which passed off without complication. She had borne no children. A number of years before, Dr. H. C. Cowles of New York had extirpated a bartholinian gland for gonorrheal infection, and in 1927 he removed the right adnexa, which were similarly diseased. The patient said that in 1927 there was a period when her legs became swollen without known cause. When I saw her, the swelling had completely disappeared.

In June, 1929, Dr. Charles Gordon Heyd operated on her for cystic disease of the left ovary, removing a degenerated multilocular intraligamentous ovarian cyst. The operation had been difficult because of many adhesions to the hollow viscera, but the remainder of the abdomen had revealed no abnormality. Pathologic examination failed to show malignant disease. At that time Dr. Heyd noted that the patient's fingers were greatly clubbed, and that the nails were incurvated. On examining her chest, signs resembling those of encapsulated fluid were discovered, and an exploratory puncture anteriorly resulted in the withdrawal of a little blood. The patient then stated that she had had pleurisy in her early youth and that it was a long time in healing. This statement is, of course, indefinite.

For a few years before I saw her she had had occasional spasmodic cough and had expectorated considerable quantities of tough mucus, sometimes flaked with blood. The attacks were asthmatic in character, but the wheezing was said to disappear on recumbency.

Examination.—The patient was a tall woman in good general condition. The blood pressure was 135 systolic and 65 diastolic, but the vital capacity was only 2.2 liters, although her normal weight was 185 pounds (83.9 Kg.).

Physical examination disclosed that in the lower half of the left part of the chest both front and back, there were the usual signs of encapsulated fluid. There was also great limitation in the extension of the right shoulder with the characteristic tenderness of subacromial bursitis. Although I did not believe that this had anything to do with the condition of her chest, I advised roentgen examination, which was carried out by Dr. Leopold Jaches. He found the right shoulder to be normal. In the chest, however, there was a large area of localized density on the left side extending from the level of the second interspace in front almost to the diaphragm, but with a small clear space between the diaphragm and the opacity. Stereoscopically, this opaque region seemed to be limited to the anterior part of the chest, and Dr. Jaches thought that the lower half of the upper pulmonary lobe was involved. There was pleural thickening and almost complete obliteration of the costophrenic sinus by what seemed to be a small quantity of fluid. The heart and other mediastinal organs were displaced

1. The cases are not arranged chronologically.

Fig. 1 (case 1).—Roentgenogram taken on Dec. 6, 1929, before operation with the patient in an erect position. The shadow resembles that of encapsulated fluid or tumor.

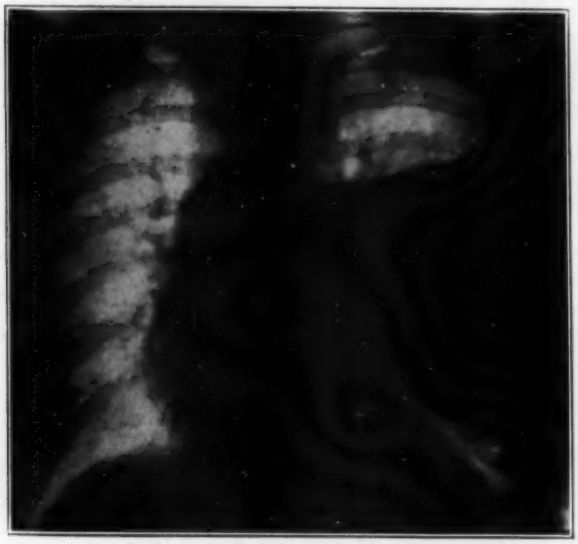

Fig. 2 (case 1).—Roentgenogram taken on the same date as figure 1 with the patient in the supine position. The print was made with Bucky's diaphragm. Note the clear space between the intrathoracic shadow and the diaphragm.

to the unaffected side, and the left border of the heart could not be seen. There was no visible abnormality in the upper left part of the chest and none on the right side (figs. 1 and 2). The aorta was normal. The right side of the diaphragm was restricted in its excursions. Dr. Jaches held the opinion that the density was probably produced by a tumor mass, but the presence of encapsulated fluid could not be excluded.

On auscultation, occasional squeaking dry râles were heard in both sides of the chest. It was evident to me that a full surgical exploration of the left side of the thorax should be made, but in order to gain as much information as possible I requested Dr. M. C. Myerson to examine the bronchial tree by endoscopy. He did this on Dec. 12, 1929, and, except for a slight bulging of the posterior wall of the bronchus of the left upper lobe into the lumen, nothing

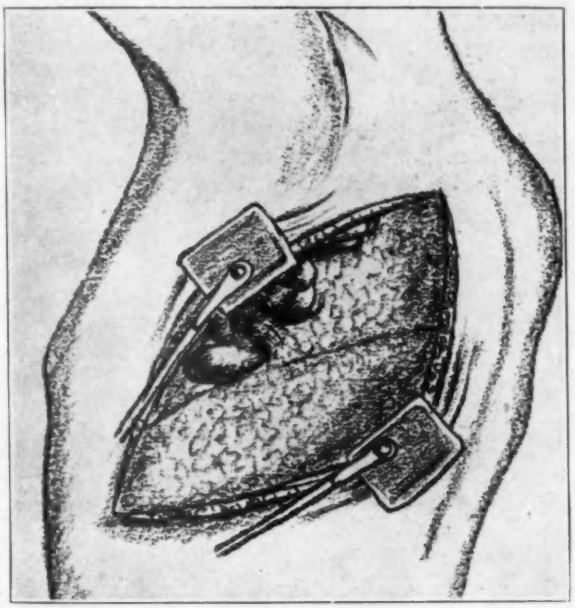

Fig. 3.—Position of the tumor in case 1. The lung is shown running on to the surface of the growth. This sketch shows the posterior part of the tumor only. The ends of two ribs which were divided posteriorly are seen above. For simplicity's sake, only one rib spreader is shown in this picture; two were actually used.

abnormal was found. Dr. Myerson said that this deformity might have been congenital.

Considering this examination, I felt encouraged to operate in the hope that I might be able to extirpate a tumor or drain a chronic encapsulated empyema.

Operation.—On December 24, the operation was performed. The anesthetic chosen by Dr. William Branower was a mixture of nitrous oxide and ethylene —no ether. Dr. Ira Cohen assisted, and Prof. Richard H. Meade of the University of Virginia, was present as an observer. The patient was placed on her right side, and the table was broken so as to widen the interspaces.

An incision of 7 inches (17.7 cm.) was made between the eighth and ninth ribs, and immediately there was a gush of clear fluid from the pleura, so that at first I suspected that there was merely a sacculated pleural effusion. The rib spreader was put in, however, and at once a large tumor was revealed, pinkish gray in color and lying toward the mesial side of the lower portion of the upper pulmonary lobe (fig. 3). The tumor appeared to have its origin in the edge of the lung. During my exploration, bleeding began from points that I could not see and, although this was not immediately alarming, it was disturbing in view of the contemplated radical procedure. It forced me to enlarge the incision and also to remove about 8 inches (20.3 cm.) of the ninth rib for better exposure. The eighth, seventh and sixth ribs were divided posteriorly, the incision having been extended upward. Finally, two rib spreaders in different parts of the wound gave ample space for full intrathoracic manipulation. Minor adhesions were peeled away, and the tumor together with a small piece of the pulmonary edge was removed, the lung being divided distal to catgut ligature (fig. 4). A large fleshy adhesion to the pericardium was ligated and cut through after the lung had been resected. The principal trouble was with the anterior adhesion that sprang from a point near the internal mammary artery, and which bled persistently so that the source had to be exposed by cutting the seventh rib near its cartilage. At Dr. Ira Cohen's suggestion, a bit of free muscle was

Fig. 4.—The specimen in case 1 after hardening. At the right is part of the lung which was resected. The mass near the center represents the stump of adhesions to anterior thoracic wall.

placed against this bleeding area, and the oozing promptly ceased. All parts of the chest were now carefully explored by vision, but the only remarkable thing to be noted was the persistent collapse of the upper lobe which refused to expand even on intrapharyngeal pneumatic pressure. I regarded this as probably the result of the long continued compression by the tumor.

A solution of dextrose, 1,800 cc., was injected into the vein of the right arm, and this was followed later by transfusion of 600 cc. of citrated blood by Dr. Nathan Rosenthal, more as a prophylactic measure than as one of emergency.

The wound was closed with pericostal sutures of chromicized catgut, and the soft parts were sutured with silk, airtight. A small intercostal incision was made in the ninth space through which a fenestrated valve drainage tube emerged.

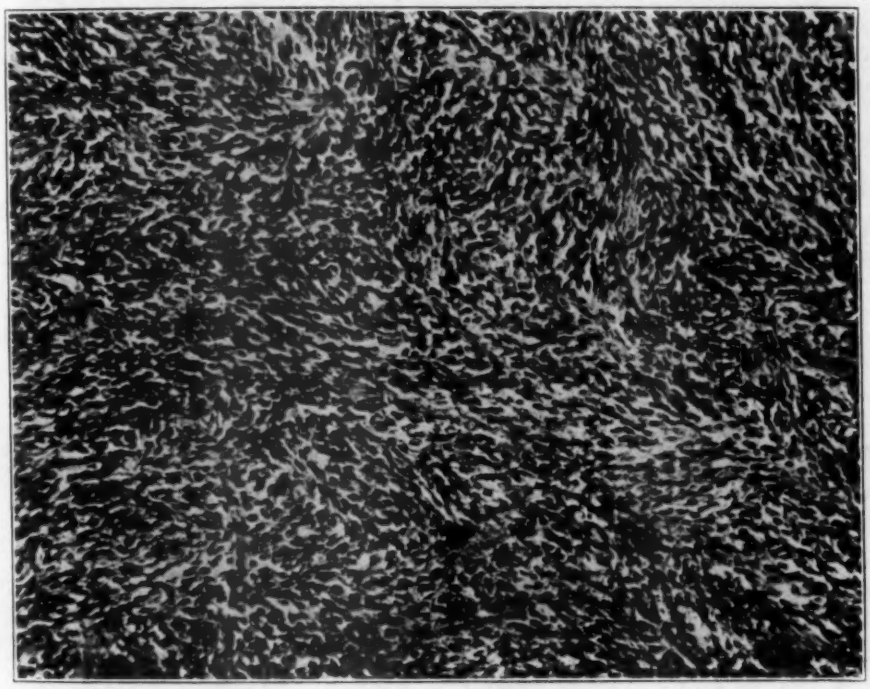

Fig. 5.—Histologic slide from the specimen in case 1.

Course.—During convalescence, which at first was far from smooth, it was rather alarming to hear the sonorous râles in both sides of the chest which made one fear that a double bronchitis was present. The pulse, however, remained of excellent quality, and the patient's good general condition was maintained. Six days after the operation there was distress in breathing with some increase in the rapidity of the pulse, and fluoroscopy revealed a sacculated hydropneumothorax in the upper part of the chest. With the patient under nitrous oxide and oxygen, I reopened the lower half of the main wound and pushing away adhesions I opened a completely closed cavity containing air under pressure and about 1,000 cc. of clear fluid.

In explaining this tense pneumothorax, I concluded that I was not dealing with a valvular condition, but that the tension was produced by the formation of a large quantity of fluid in the upper part of the chest where air had become encapsulated in the space left by the collapsed upper lobe. With the increase in fluid, the air was placed under tension. A small pulmonary fistula developed about ten days after the operation, and a low grade empyema resulted. The pleuropulmonary fistula closed spontaneously.

It is not necessary to go into further details of the convalescence. It was slow, and at the time this paper was written there was still a pinhole over which a tiny piece of gauze with one bit of adhesive plaster was worn as a dressing. The roentgenogram, however, indicated a sacculated pneumothorax and pleural thickening (fig. 6). I fancy that nature will eventually bring about complete

Fig. 6 (case 1).—Four months after operation. At this time the wound was a tiny fistula from which about two drops of fluid exuded in twenty-four hours; yet there was considerable lateral pneumothorax and thickened pleura. The patient was practically well. There seemed to be an upward dislocation of the third rib, probably due to the transmitted force of the rib spreader.

obliteration of this air-filled space, though it is possible that an aseptic air pocket may remain for years, with no evil effect.

As a somewhat distressing complication, a number of teeth had to be extracted because of infection of the apical roots. Both shoulders were painful, and the subacromial bursitis had not entirely disappeared four months after operation, although the patient was in good general health and was gaining in weight.

NOTE.—Now, more than seven months after the operation, the wound is soundly healed and the patient writes that she is in excellent health.

CASE 2.—*History.*—Max B., aged 55, had been complaining for about two and one-half years of pain in his chest with remissions and recrudescences. There had been neither cough nor other distinctly pulmonary symptoms, but he had shortness of breath on exertion. The physical signs had been those of solidification in the lower left part of the chest, where there was a distinct bulging of the thoracic wall backward and outward. Fever had been absent, but there were general deterioration and progressive weakness. Roentgen examination revealed a semicircular shadow about 6 inches (15.2 cm.) in diameter in the lower left part of the chest (fig. 7). Dr. George Woolsey, who referred the patient to me, had operated about ten days before I saw him, resecting the ninth, tenth and eleventh ribs over the tumor. The mass proved to be extremely solid, and one rib was greatly broadened but not neoplastic. A cleavage plane permitted a specimen the size of a golf ball to be removed, and this was pronounced neurofibroma after examination in the laboratory of Roosevelt Hospital. Examination

Fig. 7 (case 2).—Roentgenogram taken before operation showing the enormous fibrosarcoma of the lower left side of the chest.

by an outside pathologist resulted in a diagnosis of fibroma or possibly fibrosarcoma of a low grade malignancy (fig. 8).

At my suggestion, the patient was treated by injections of erysipelas and prodigiosus toxins (Coley's) which he bore well so far as his general nutrition was concerned, but the reactions depressed him so that after a few weeks this mode of therapy was omitted.[2]

There was general improvement, but about five months later I perceived a slight fetid odor at the patient's mouth and, fearing that there might be interference with bronchial drainage, I advised that the tumor be shelled out of its capsule if possible, and that the injections of the toxins be resumed.

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2. My reason for advising the toxic treatment was that I had had success in many cases of sarcoma with this form of therapy, and because Dr. Woolsey's description of his operation was not one which would make the surgeon anxious to attempt extirpation.

Operations and Course.—The patient entered the Private Pavilion of Mount Sinai Hospital, and on Nov. 23, 1926, I operated, using nitrous oxide and oxygen as an anesthetic. The operation proved beset with difficulties and could not be carried out as projected.

An incision about 6 inches (15.2 cm.) long was made through the old scar. Bleeding was considerable, and it was difficult to resect the ribs on account of the trouble in securing the anomalous vessels in the tissues surrounding the tumor. Two ribs were finally resected, and the dense mass beneath was reached. I succeeded in removing a mass only about the size of a lawn tennis ball, and was then forced to desist because of large vessels which might have been injured within the depths. The case was obviously not radically operable. The

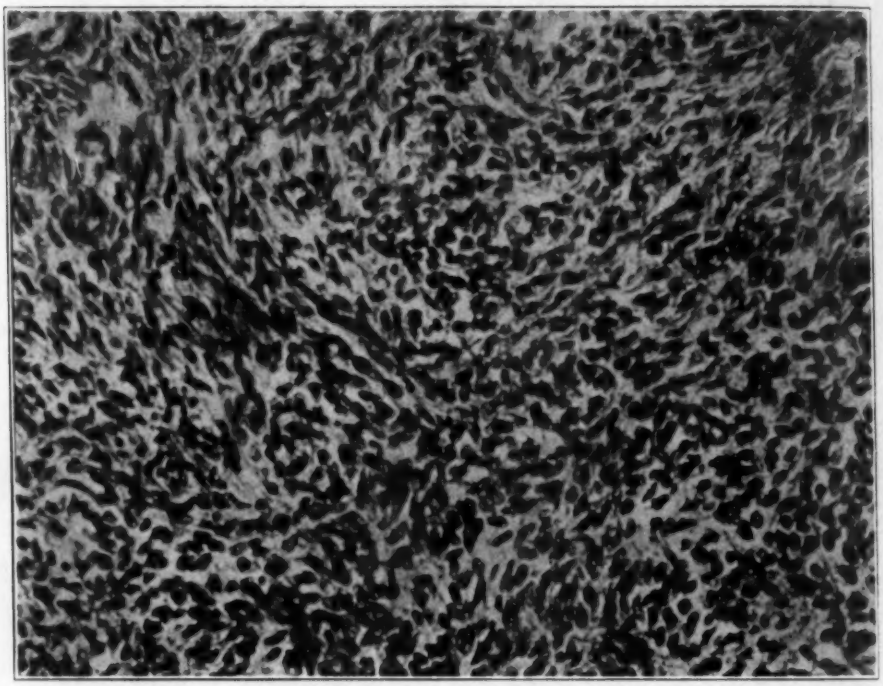

Fig. 8.—Photomicrograph of tumor in case 2, removed at the second operation.

hollow was firmly packed with gauze, and the skin was closed over it by temporary sutures. These were removed three days later, and when the packing was removed smart hemorrhage appeared in the depths so that gauze had to be immediately replaced, this time soaked with thromboplastin. The patient's pulse rate, which was 80 before the operation, dropped to 76 twenty-four hours later. Pain was absent. I had hoped to remove more of the tumor with the aid of the diathermy monopolar knife but the electric appliance cut altogether too slowly for this kind of operation.[3] Roentgen therapy was then administered by Dr. William Harris through the wound, and later on, another course of erysipelas and prodigiosus toxins (Coley's) was begun, but had to be abandoned because of the patient's complaints.

3. A more active cutting electric blade is now available.

The wound healed from the bottom, and Mr. B. stated that his respiratory distress had been materially improved. He soon was up and about once more attending to his business.

Almost three years later, in February, 1929, the patient's weight was 120 pounds (54.4 Kg.). His vital capacity was 2.8 liters. His blood pressure was 145 systolic and 85 diastolic. Roentgenograms revealed a shadow about as it was before my operation.

On April 1, 1930, the patient came to me again. He now weighed 8½ pounds (6.8 Kg.) more than the previous year, but his vital capacity had dropped 0.6 of a liter (to 2.2) while the blood pressure had risen to 165 systolic and 90 diastolic. It is, however, recognized that in the case of this man, a sensitive person, the blood pressure readings at the office were probably higher than those of the patient's normal tension because of nervous apprehension.

I now found a rather puffy area over the posterior part of the tumor. There was slight cough but no expectoration. The general appearance was distinctly better than it had been. He again entered the hospital, and on April 24, 1930, I incised the old scar with a diathermy knife, easily shelling out the external softer part of the tumor which was of an entirely different consistency from that of the original new growth. With considerable physical effort, I then managed to enucleate a portion of the old tumor which was now extremely hard, and even seemed to be in some regions calcareous. The entire mass removed was about the size of a man's fist.

Pathologic Report.—Dr. Klemperer's report on the specimen is as follows: soft portions, "Polymorphus cell sarcoma with necrosis"; firm portions, "hard fibroma."

"The soft portions of the tumor consist of very cellular areas in which the nuclei vary extensively regarding their size and chromatin contents. The paler nuclei resemble nuclei of fibroblasts, there are quite frequently cells encountered with very large intensely stained nuclei, often with two nuclei. The cellular areas blend with less cellular areas with abundant intercellular ground substance, but also here the irregularity of the cellular elements is very conspicuous. There are wide areas of necrosis and in the neighborhood of these, the tumor elements show a peculiar transformation whereby they become enormously enlarged with a bluish halo surrounding the markedly shrunken cells, the structure resembling cartilage. It is very possible that this is only a degenerative phenomenon. The intercellular substance is fibrillar and stains pink.

"The firm portions of the tumor are composed of a very dense tissue, very poor in cellular elements which resembles in its appearance the structure of a tendon. Here and there, however, one finds more cellular areas which also show a good deal of irregularities. The present tumor shows considerable differences from that removed several years ago which was a neoplasm of a uniform appearance."

The tumor, therefore, had undergone a great change for the worse. On roentgen examination, a circular shadow, probably that of a metastasis, was found in the contralateral lung (fig. 9).

INCIDENCE

Giant sarcoma of the pleura or, more accurately, of the subpleural tissues, is extremely rare. The diagnosis is usually made on postmortem examination.

Klemperer and Rabin,[4] who collected a great mass of evidence from the literature, and who added cases personally observed by them, spoke of the solitary or localized form of subpleural connective tissue tumors. There seem to be two types; one, that of small tumors arising from the edges of the lungs, usually innocent small masses found at autopsy and not contributing to the fatal issue. There are also found in this region chondroma, fibroma and lipoma. The other is of a type which grows to gigantic proportions, even filling the chest, and causing death by mere bulk through circulatory disturbance. One case cited was that of a tumor 7 pounds (3.2 Kg.) in weight. These tumors usually originate beneath the costal pleura, my own case here reported (case 1), being

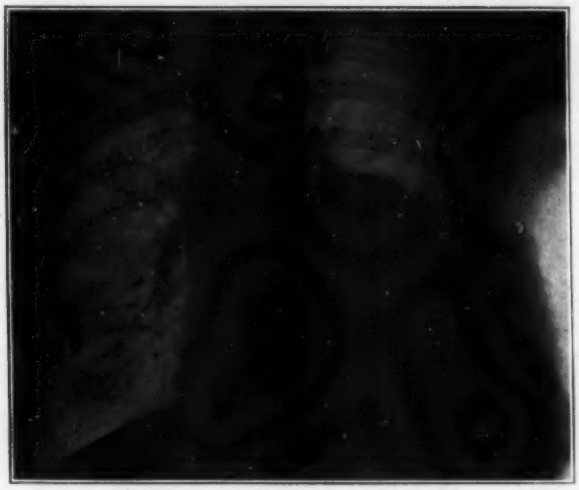

Fig. 9 (case 2).—Roentgenogram taken four years later, and immediately following third operation. The iodized oil gauze packing is faintly seen. There is now a secondary tumor in the opposite lung.

one of the rare exceptions and beginning on the visceral side, as in the case of the small tumors of accidental discovery. This type rarely, if ever, produces metastases in spite of the sarcomatous histologic appearances. Only twelve of these cases have been unearthed by Klemperer and Rabin, and a tabular study of these may be found in their paper.

My first case was typical in that the tumor was covered by what seemed to be an extension of the visceral pleura. It was nodular (fig. 4). Microscopically, the appearances were those of fibrosarcoma

4. Klemperer, Paul, and Rabin, Coleman B.: Neoplasms of the Pleura-Mesothelioma and Fibrosarcoma, read at the 1930 meeting of the American Association of Pathologists and Bacteriologists. Dr. Rabin furnished me with data from his notes.

or fibroma with comparatively few tumor cells. Adhesions to surrounding structures were present, and in my second case, the exact origin of which could not be proved, the diaphragm as well as the pericardium was firmly adherent. This is the one which later changed its character, both clinically and histologically, and which produced a metastasis (fig. 9).

COMMENT

At the 1923 meeting of this association, when I was president, the subject of my address was "Malignant Tumor of the Lung, and Necessity for Early Operation."[5] In this paper I earnestly stressed the need for prompt intervention according to the surgical principles generally accepted in dealing with tumors elsewhere in the body. This was seven years ago, and the fellows of the association have shown diligence and interest in the study and surgical management of thoracic tumors. The association itself made a step forward by organizing a registry of neoplasms of the chest from which we shall certainly learn much. Yet the medical profession at large is slow to follow our lead, and it persists in the futile course of treatment by diagnosis, even to the final melancholy chapter of the postmortem report.

I have presented here two cases which speak for themselves. That the condition in both was histologically malignant merely emphasizes the validity of arguments for early and radical action. I will state here briefly a few apparently self-evident propositions associated with this subject, and will give my conclusions:

1. All tumors should be diagnosed.
2. Tumors may be classified as malignant or innocent.[6]
3. Tumors that are malignant should be extirpated.
4. Tumors that are not malignant but that interfere with normal life, or with the happiness or welfare of the host, should be eliminated.
5. An operation or other procedure that is more dangerous than the condition which it would relieve is unjustifiable.
6. Intercostal diagnostic exploration through the normal thoracic wall, when performed under the principles of thoracic surgery, is not an extrahazardous operation.[7]
7. Exploratory laparotomy is performed frequently with the consent of the internist or even at his suggestion.

If the foregoing propositions are accepted, diagnostic operative procedures on the thorax should be the rule in the case of a tumor within the cavity of the chest, unless it is possible to learn its nature by other methods such as endoscopy or the biopsy of a metastasis.

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5. Lilienthal, H.: Malignant Tumor of the Lung: Necessity for Early Operation, Arch. Surg. **8**:308 (Jan.) 1924.

6. The word nonmalignant may be used, but the designation of any abnormal growth as benign is erroneous.

7. It entails less shock and a far shorter period in bed than a laparotomy of equivalent magnitude.

8. A symptomless mass accidently discovered by routine roentgenology does not, of course, demand immediate intervention even for accuracy of diagnosis; but repeated observations should be made, and any increase in size or any onset of symptoms should be the signal for full investigation including, if necessary, exploratory operation. One may come on an essentially innocent growth, at the time removable, which, if left to itself, would increase in size and become hopeless.

A most instructive instance was presented at the pathologic conference of Mount Sinai Hospital on April 23, 1930, which profoundly impressed me. A man of middle age had entered the hospital eleven years before with signs of some endothoracic disturbance which led to roentgen examination. This revealed a clinically benign type of tumor

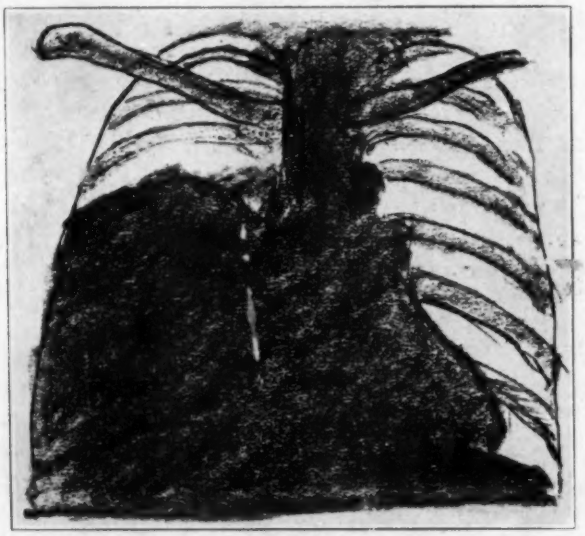

Fig. 10.—Huge lipoma of the lung, mistaken for cancer (clinically not roentgenologically). This is a rough sketch merely to give an idea of the size of the tumor at that time. (Tracing from Wessler and Jaches' Clinical Roentgenology of Diseases of the Chest, The Southworth Company, 1923.)

of the lung, probably involving the pleura. The patient had been in good health for over one year (fig. 10).[8] A little bloody fluid was withdrawn from the chest by aspiration, and the conclusion reached was that the patient was suffering from cancer of the lung.

This decision was strengthened by the presence of one or two vague shadows which were thought to indicate metastasis. After a number of years the man presented himself, only a short time before his death, with an enormous tumor producing embarrassment of the right side of

8. Wessler, H., and Jaches, Leopold: Clinical Roentgenology of Diseases of the Chest, Troy, N. Y., The Southworth Company, 1923, p. 299.

the heart, from which he succumbed. The case was presented by Dr. George Baehr. The specimen demonstrated by Dr. Paul Klemperer was that of a gigantic lipoma arising in the subpleural tissue (fig. 11). The state of the patient at his last admission forbade even minor diagnostic surgical measures, but surely eleven, or ten, or perhaps from five to three years before his last admission this tumor could have been removed or resected with little risk. Indeed, nothing would have been

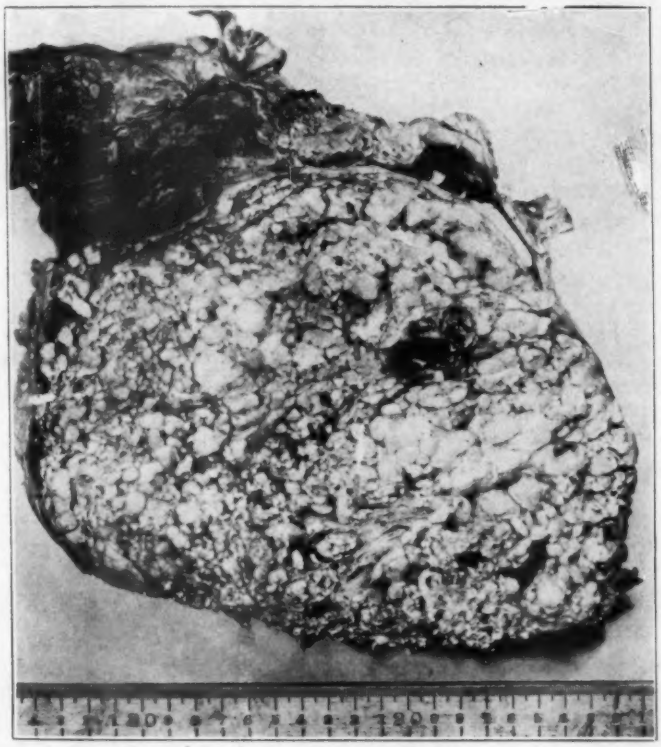

Fig. 11 (case 2).—Postmortem specimen eleven years later. (With permission of the Pathologic Department, Mount Sinai Hospital.)

lost had an operation been undertaken for the sake of certainty at the time of his first examination. The fact that the man lived for so long a time with gradually increasing distress was not a reason for inaction.

Were this address intended solely for the fellows of this association, my presentation of the subject for a second time would be inexcusable. But my words will be read by others, and the paper may, perhaps, be abstracted by journals, so I trust that its message may be carried far beyond these walls.

ABSTRACT OF DISCUSSION

DR. C. G. HEYD, New York: The case that Dr. Lilienthal has presented is of great interest by reason of the fact that the patient has been examined by at least six physicians. She was referred to me for a pelvic condition, and on doing a routine examination, I was impressed with the tremendous clubbing of the fingers. They were almost like the drumstick of a chicken. How it could be possible for the five physicians who examined her before I did not to note these fingers is rather surprising. Before she was operated on for the pelvic condition, roentgenograms of the chest were taken which showed the tumor exactly as Dr. Lilienthal has indicated in his pictures. We were then in a difficult position. She had come to me for a pelvic condition. I did not disclose the tumor of the chest until after she had had a bilateral ovarian cyst removed. She made an uneventful convalescence from the laparotomy, and then we apprised her of the condition of the chest. Roentgenograms were taken in numerous positions, and the roentgenologist could not state what he thought the tumor was. I should like to ask Dr. Lilienthal if a preoperative roentgen diagnosis as to the character of the tumor was made.

DR. HOWARD LILIENTHAL, New York: No.

DR. C. G. HEYD: That was our difficulty. At about the same time one of our nurses came to me because of a goiter; she exhibited almost the same clubbing of the fingers, only not to such an extent, and she had a shadow almost identical with that which the patient presented. We told her that the condition of the lung was of far greater significance than the goiter. The result was that she had nothing done and is still going about her duty with a progressive enlargement of the fingers.

It is a distinct pleasure to have followed this case of Dr. Lilienthal's, and it is surprising to note the apathy of the medical profession in regard to lung pathology as the physician sees patients with clubbed fingers from time to time, which are an open invitation for an investigation of the chest. I congratulate Dr. Lilienthal on his excellent result.

INTRATHORACIC TUMORS

REPORT OF CASES

T. C. DAVISON, M.D.
ATLANTA, GA.

It is not my intention to present in detail a textbook discussion of tumors of the chest, but after a brief general discussion of the subject to report a series of cases that have occurred in my private practice and that have been observed at the Steiner Clinic of Atlanta. Intrathoracic tumors are more common than formerly reported, and are divided into primary and secondary.

Primary tumors may be benign or malignant. The benign group, including lipoma, chondroma, osteoma, fibroma, fibropapilloma and dermoids, is rare. Benign tumors may occur in the mediastinum or in the lungs. The diagnosis of nonmalignancy cannot be made at once but only after prolonged observation, when, if the tumor has not increased in size and if it retains its regular sharp outline, with no increase of symptoms, a diagnosis of nonmalignancy may be made. Benign tumors may produce pressure symptoms that are distressing, and at times pulmonary suppuration and sepsis by partial or complete obstruction of the bronchi. In the malignant group, carcinoma is the most frequent. Statistics by various authors as to its incidence vary from 1 to 10 per cent of all cancers. Certainly a higher percentage is being diagnosed now than was formerly thought to exist. This may be the result of more thorough examination and the more frequent use of the x-rays and the bronchoscope. Primary carcinoma of the lung may be endobronchial or parenchymatous, the bronchial type being the more common. It occurs more frequently in males than in females, the ratio being given by Fishberg as 2:1, and other authors estimate an even higher ratio. Chronic irritation must be considered as the principal cause of primary cancer of the lung, this being produced in many cases by the inhalation of irritating substance, such as dust by miners and stone cutters and irritating gases and tobacco smoke. Chronic bronchitis, tuberculosis, asthma and influenza may be forerunners of cancer of the lung. It at times occurs in connection with pulmonary abscess and bronchiectasis, and it is impossible to say which is cause and which is effect. Cancers of the lung occur most often late in life or after 60 years of age, but they have been observed in young adults. Ewing reported 80 per cent as occurring in the upper lobes of the lungs. The pathologic process may invade the contiguous tissues and organs by infiltration, and by partial or complete obstruction may result in bron-

chiectasis, atelectasis, gangrene, abscess, empyema and hemorrhage. The tumors may metastasize through the lymph or blood stream to any portion of the body. Tuffier believed that metastasis takes place early; this is not concurred in by others. The most frequent locations of metastases from primary cancer of the lung are the bronchial glands, liver, bones, brain and cervical and thyroid glands.

Practically all secondary tumors of the lung are malignant and are metastases deposited by the blood and lymph streams in the pulmonary parenchyma from some distant primary focus. They may be single or multiple and grow into spheroidal masses which may reach great size and retain their sharp outline for a long time. The course of secondary carcinoma of the lung is somewhat similar to that of primary, only it is usually more rapid, as the patient probably has already become anemic and depleted by the primary condition. The signs and symptoms of cancer of the lung are not very different from those of other pulmonary conditions, but they tend to persist and progress in spite of treatment. The symptoms at first may be rather vague and indefinite, more of a sensation of gradually increasing ill health, with slight cough. Later there is pain in the chest, which may be referred to the shoulder and down the arm on the affected side. The cough becomes increasingly productive and more severe. The sputum may be slightly streaked with blood, but has no fetid odor. The physical signs may be misleading even in advanced cases. Usually they resemble the signs of tuberculosis, unresolved pneumonia or fluid in the pleural cavity. There may be some elevation of temperature even before a mixed infection is present. Tubercle bacilli are sometimes found in the sputum, as the two conditions may coexist. The blood is not characteristic; there is usually a moderate leukocytosis, but anemia frequently develops late. Clubbing of the fingers and toes is present in many cases, particularly if there is bronchiectasis or abscess as a complication. The diagnosis, as a rule, cannot be made from the history and the physical examination alone, but these are very important. The bronchoscope is a valuable aid in diagnosing pulmonary tumors and should be used early in cases in which tumor is suspected. It is not a dangerous procedure, and should not be reserved for use as a last resort.

Many of these tumors have their origin in the mucosa of the bronchi, and a fragment from a suspected area can easily be removed for biopsy through the bronchoscope, thus clearing up the diagnosis. This can often be done before the x-rays show anything definite. Roentgen examination has been our chief aid in diagnosing tumors in the thorax; it has often revealed the presence of tumors that were not suspected. In cases in which a tumor is thought to be present, both anteroposterior and lateral views should be made. Fluoroscopy should be done in all

cases. Sarcomas are hard to differentiate from carcinomas and are only one-fourth as frequently observed.

In every case in which thoracic tumor is suspected, a careful history should be taken and a thorough physical examination made with the idea of locating any obscure primary focus or metastatic nodules from which microscopic specimens may be obtained for diagnostic purposes.

Roentgen therapy has been used extensively in cases of suspected and proved malignant tumors of the mediastinum and lungs. It usually has a palliative effect, causing temporary improvement. Occasionally a case is reported clinically diagnosed as malignant which has responded readily to roentgen irradiation. Schroeder of Cincinnati reported such a case with remarkable recovery, and the roentgenograms appear in Dr. Lilienthal's book. At the Steiner Clinic in Atlanta, roentgen therapy is used as a routine measure for its palliative effect only.

Surgical intervention offers the only hope for recovery from an early neoplasm of the lung. After removal of the tumor-bearing area, healing should occur without infection. The so-called dead space is obliterated by the elevation of the diaphragm, the contraction of the thoracic wall and possibly by a physiologic emphysema of the remaining pulmonary tissue.

In selecting patients for operation, the bronchoscope and the x-rays should be the main guides. The location of the tumor in the lung will also influence the operator's decision, those in the periphery being more accessible than those located nearer the bronchial tree. The end-results depend on how early these cases come to operation, and unless the surgeon has the sympathetic cooperation of physicians, patients with malignant tumors of the lung will continue to reach the surgeon too late for cure. In extensive operative procedures on the lungs, Sauerbruch advises a two stage operation. At the first, the necessary rib resection is done and the pulmonary artery controlling the affected lobe is ligated. At the second stage, three or four weeks later, the diseased area is extirpated.

In late cases, palliative operations may be performed on selected patients, such as partial collapse of the affected lung, evacuation of secondary abscess of the lung and resection of a large portion of the tumor, which in certain cases may give temperorary relief from distressing symptoms.

In operations on the lung, its vascularity is somewhat of a handicap. The high frequency radio-knife and coagulator can be used to advantage. Lilienthal advises exposure of the tumor, curetting or scooping out of the contents and packing with gauze. The gauze is left in place several days and then changed daily. Slough will be cast off, and later the area can be treated with the x-rays or radium.

REPORT OF CASES

CASE 1.—(Case reported to the Fulton County Medical Society by Dr. R. S. Leadingham, pathologist to Grady Hospital.) A white man, aged 20, was admitted to the Grady Hospital on Feb. 7, 1930. The chief complaints were orthopnea, cough and edema of the lower extremities. As the patient was admitted to the hospital acutely ill, no history was attainable.

Examination revealed enlarged cervical glands. The patient was somewhat cyanotic and unable to lie down on account of difficult breathing. Mediastinal dulness extended from the right sternal margin to the left axilla. There were

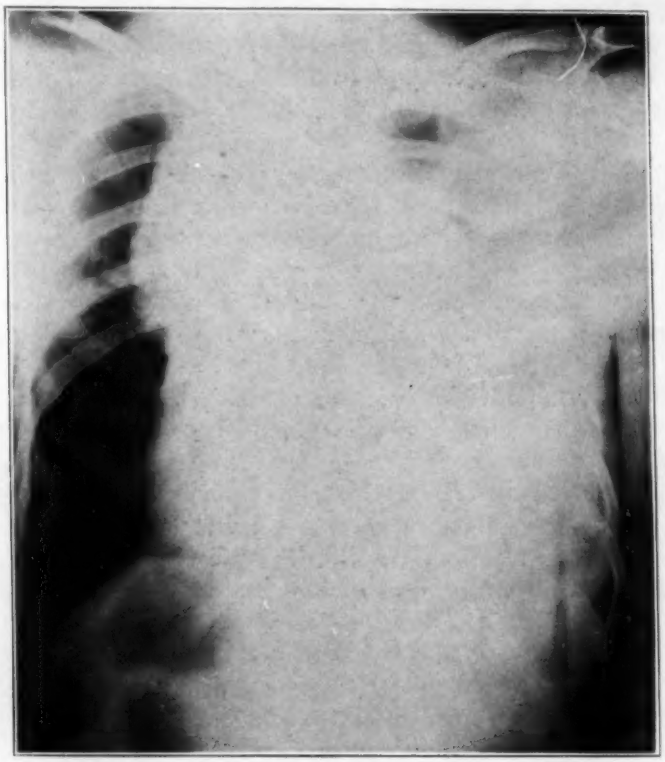

Fig. 1 (case 1).—Lymphosarcoma of the thymus gland.

moist râles over the bases of both lungs. The heart sounds were muffled, and there was a soft systolic murmur at the point of maximum impulse. The pulse rate was 120 and regular, and the volume was fair. The systolic blood pressure was 122 and the diastolic 84. The temperature on admission was 98.4 F., and the respiratory rate, 24. The white blood cells count was 17,000, with 68 per cent polymorphonuclears. Roentgen examination showed a large tumor mass occupying a greater portion of the left side of the chest and mediastinum, displacing the heart to the right.

Twelve hours after admission the temperature was 102 F. and the pulse rate, 120. The patient died suddenly four hours later.

At autopsy, a large mediastinal mass was found extending from above the clavicle to the superior surface of the heart and displacing both the heart and the great vessels. Microscopic sections showed lymphosarcoma of the thymus gland. The lymph nodes of the mediastinum and retroperitoneal regions were enlarged, and there were several soft nodular masses in the right lung. On the surface of both kidneys there were single small nodules 1 cm. in diameter. No metastases were found in other tissues of the body. There were scattered areas of bronchopneumonia in both lungs.

Fig. 2 (case 1.)—Gross specimen of figure 1 showing heart and blood vessels displaced downward by the tumor.

CASE 2.—Mrs. V. S., aged 53, married, was admitted to the Steiner Clinic on Jan. 17, 1930, with the complaint of pain in the back and the left side of the chest and a tumor on the left side. The present illness began about eighteen months before admission, when the patient noticed a pain in the side and back; it was intermittent at first and gradually grew worse. Ten months before she noticed a lump or a tumor on the left side, just posterior to the axilla. At the time of admission the pain was in the left side near the breast and was severe. The patient took six acetylsalicylic acid tablets daily for relief.

She had had the usual childhood diseases. She had had an operation for ovarian tumor (?) when 20 years of age. The menopause occurred when she was 47.

Her father died of nephritis and her mother died at 60 of "rheumatism," but had had an operation for tumor of the breast four years previously.

The tumor presented by the patient was small (3 by 4 by 2 cm.); it was located in the left posterior axillary fold, and was not attached to the ribs. It was not tender on examination. There were palpable glands in the left axilla and supraclavicular space, but none on the right side. A roentgenogram, taken on January 17, showed the tumor in the left axillary region with destruction of a portion of the sixth and seventh ribs, probably a cyst producing pressure necrosis.

Fig. 3 (case 2).—Myxo-angio-endothelioma showing destruction of the sixth and seventh ribs.

There were 3,760,000 red blood cells, 70 per cent hemoglobin, 8,050 white blood cells and 65 per cent polymorphonuclears, 31 per cent being small. The results of urinalysis were essentially negative.

On March 24, 1930, a section from the wall of the cyst showed myxo-angio-endothelioma, evidently arising from the pleura.

A diagnosis of myxo-angio-endothelioma was made. Roentgen irradiation, five treatments, was given in January and February, with no improvement.

A recent roentgenogram showed that the disease was progressing rapidly in spite of treatment. The patient is still under observation.

Case 3.—Mr. J. T., aged 60, complained of cough, raising of sputum, anorexia and loss of weight for a period of two months. There was no family history of cancer. He had never had pneumonia, bronchitis, asthma or any thoracic disease, and had been well until the present illness. He had had three severe head colds three months before the onset of the present symptoms, but did not go to bed. Loss of appetite began with a cough, and at this time he began to lose weight. He had no pain at any time. Four months after the onset, the cough and loss of weight had progressed greatly, and he raised a large quantity of foul sputum. He then came to the hospital, where he was kept continually in bed. The odor of the sputum became worse. The temperature reached 100 F. daily. The measured amount of sputum was from 200 to 500 cc. in twenty-four hours; respirations ranged from 22 to 26, and the pulse rate from 88 to 108; the urine was normal, and the leukocytes on admission to the hospital numbered 18,000. Two

Fig. 4 (case 3).—Primary carcinoma of the lung, coexisting with abscess.

months later they were 32,000; the red blood count was 2,800,000, and the Wassermann reaction was negative.

A diagnosis of abscess of the lung was made. Drainage was established, and 60 cc. of very foul pus was obtained. The patient died three days later. Partial necropsy revealed primary carcinoma of the lung.

Case 4.—Mrs. E. F., aged 66, was admitted to the Grady Hospital on March 1, 1930, complaining of pains in the chest, hematemesis, pain in the head, cough with dyspnea and night sweats. The present illness began with pain in the epigastrium for several months. For the past three months, there had been pain in the head. On Feb. 26, 1930, the patient vomited blood, and had been spitting up some blood since. On March 1, she coughed up about "one quart of bright red blood." She had had typhoid fever at the age of 12. Both breasts were removed thirty-three years previous to admission. The patient was told that the breasts were not malignant. She had had influenza in October, 1929, and the cough had persisted since that time. The family history was unimportant.

On March 22, the red blood count was 3,530,000, with 75 per cent hemoglobin; the white blood count was 10,500. On April 9, 125 cc. of coffee-colored fluid was aspirated from the ninth interspace in the posterior axillary line. A twenty-four hour culture showed no growth. A roentgenogram on March 4 showed a large round mass in the upper left side of the chest with an opacity at the base of the left lung. The heart shadow was displaced to the right. The picture was suggestive of a new growth.

The diagnostic impression was sarcoma, cyst or syphilis.

A roentgenogram of the chest on March 26 showed increased density from the second interspace almost to the diaphragm on the left side. The density was homogeneous and was probably a new growth arising from the mediastinal region.

Examination revealed an anemic woman, apparently in constant pain. She coughed occasionally and spat bright red blood. The heart could not be per-

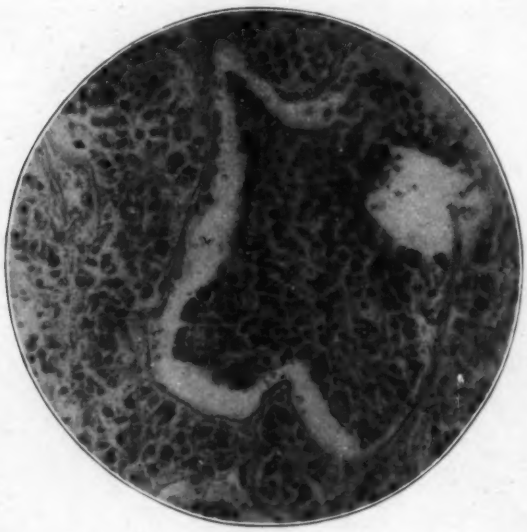

Fig. 5 (case 3).—Carcinoma of the lungs. Same as figure 4.

cussed and outlined owing to pain. There was partial heart block with an occasional dropped beat. The vessels were sclerosed. The systolic blood pressure was 85 and the diastolic 65. A systolic murmur was noted. There was a definite area of dulness and diminished tactile fremitus extending from the midline to the left thoracic wall, which occupied the middle third of the chest. Expansion on this side was definitely limited. A few fine moist râles were heard over this area of dulness. The right lung was normal.

Diagnosis of primary mediastinal cyst was made.

This patient is in the medical service, and because the blood shows a 4 plus Wassermann reaction she is receiving antisyphilitic treatment and is rapidly growing worse. The pathologic process in the lung is becoming more extensive, which, in my opinion, proves that the primary condition is not syphilitic.

Case 5.—Mr. D. H. L., aged 53, married, was admitted to the Steiner Clinic on Oct. 21, 1929, complaining of pain in the left side of the chest, yellow, foul,

frothy sputum, loss of weight and moderate anemia. The present illness began with pain in the left side, which had continued for the past fourteen years. Blood-streaked sputum had been expectorated at times, but not recently. The patient had lost weight in the past three years. He had been under treatment by various physicians and had taken antisyphilitic treatment over long period of time, with no apparent benefit. He had had pneumonia one year before admission. He had lost 50 pounds (22.7 Kg.) in the last three years.

Examination revealed a distinct bulging in the upper portion of the chest with large varicose veins over the sternum and anterior portion of the upper part

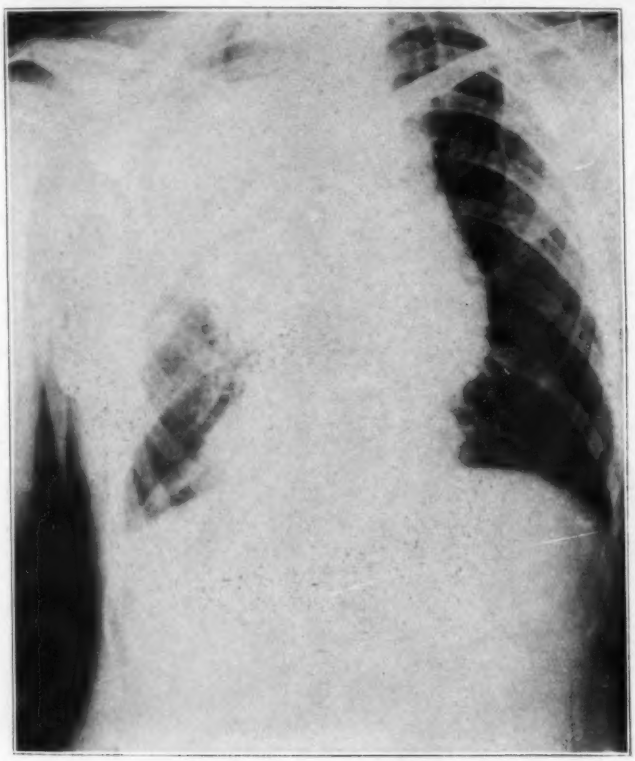

Fig. 6 (case 4).—Primary mediastinal cyst.

of the abdomen. The breath sounds, voice sounds and tactile fremitus were increased over the right side of the chest. A few moist râles were heard. There was a mass the size of a small orange in the right lower quadrant of the abdomen. The red blood count was 3,580,000, with 76 per cent hemoglobin. The urine was normal. The Wassermann reaction was negative. The roentgenogram showed a shadow, apparently enlarged glands of the mediastinum or a primary cyst, possibly a dermoid.

A probable diagnosis was made of a dermoid cyst of the mediastinum pressing on the superior vena cava.

The patient is still under observation.

Case 6.—Mrs. B. L., aged 51, married, was admitted to the Steiner Clinic on Aug. 12, 1929, complaining of polyuria and dysuria, edema, loss in weight and pain in the left side of the chest since May, 1929. The present illness began gradually twelve months before admission. The past history was unimportant, except for amputation of the breast five years before. The patient was told that it was not malignant.

Examination of the chest gave negative results. The extremities showed a clubbing of the fingers with enlargement of the joints, especially the phalangeal joints. The patient looked acromegalic. The systolic blood pressure was 132

Fig. 7 (case 5).—Mediastinal tumor obstructing the superior vena cava; varicose veins on the anterior surface of the chest and abdomen.

and the diastolic 68. The red blood count was 2,480,000. The Wassermann reaction was negative. A roentgenogram showed a sharply defined homogeneous shadow of increased density the size of a grapefruit in the base of the left lung.

The diagnostic impression was that probably a benign cyst was present. A roentgenogram of the long bones showed chronic arthritis and chronic productive periostitis. The patient died in November, 1929. Permission for autopsy was denied.

The final diagnosis was uncertain, but the condition was probably a benign cyst of the left lung.

Fig. 8 (case 5).—Same as figure 7, showing mediastinal tumor.

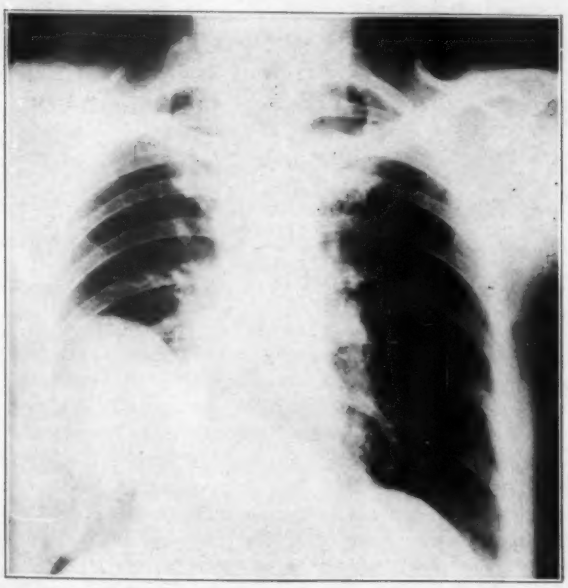

Fig. 9 (case 6).—Cyst of the lung, probably benign.

CASE 7.—A. T., a schoolgirl, aged 11, was admitted to the Steiner Clinic on Dec. 3, 1926, complaining of pain in the left upper part of the chest and general weakness. The present illness began with these symptoms, which had existed for several years and had gradually progressed. The patient was healthy until the age of 6. Her parents noticed that she was not growing as fast as her older sister; she became weak and would not play as other children. Recently, she complained of pain in the left upper part of the chest. She had had a fast pulse, and her color had not been good. A roentgenogram of the chest on March 24, 1924, showed a tumor of the mediastinum. She was given several doses of arsphenamine and also roentgen treatment before being admitted to the clinic.

Examination revealed a rather pale girl, aged 11, undernourished and undersized. There were several enlarged glands under the angle of the jaw on both

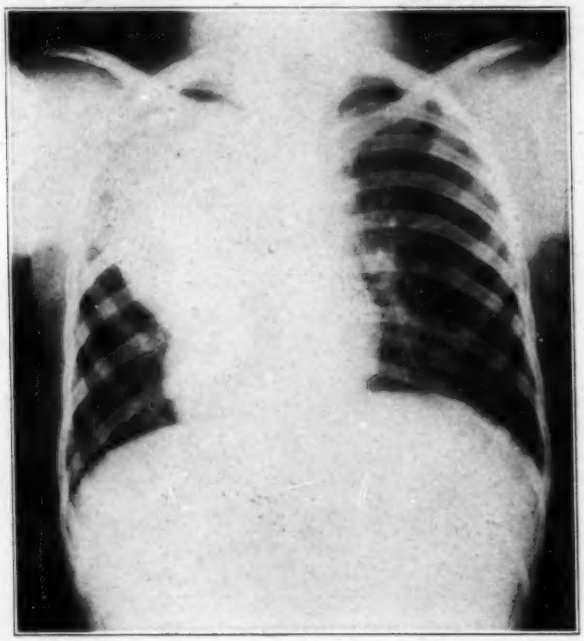

Fig. 10 (case 7).—Cyst of mediastinum of several years' duration, probably benign.

sides. The chest showed thin, only fair, symmetrical expansion, owing to pain on deep inspiration. There was slight diminution of resonance over the left scapular region and decrease in breath sounds over the same area. No râles were heard. It was impossible to outline by percussion the tumor shown on the x-ray films. The red blood count was 4,000,000, with 78 per cent hemoglobin; the white blood count was 12,850, with 61 per cent polymorphonuclears. A roentgenogram of the chest on Dec. 14, 1927, showed a large, sharply outlined spheroidal-shaped shadow or mass in the upper left side of the chest, continuous with the mediastinum. The mass on lateral exposure appeared in contact with the ribs behind.

A diagnosis of benign cyst of the mediastinum (primary) was made.

The patient is still under observation.

CASE 8.—Pat C., aged 3, was admitted to the Steiner Clinic on Dec. 6, 1929; the chief complaint was hematuria and a mass in the right side of the abdomen. The present illness began on November 24, when the patient passed bloody urine; he continued to pass it daily since that time. On December 1, a mass was noticed in the right side of the abdomen which was not sensitive or painful.

Examination revealed a large firm mass in the right side of the abdomen, extending from the lower border of the ribs to the crest of the ilium. The abdomen was slightly distended. The right kidney could not be outlined separately from the mass. The left kidney was not palpable. The spleen and liver were apparently normal. The diagnostic impression was: (1) sarcoma of the right kidney and (2) hypernephroma.

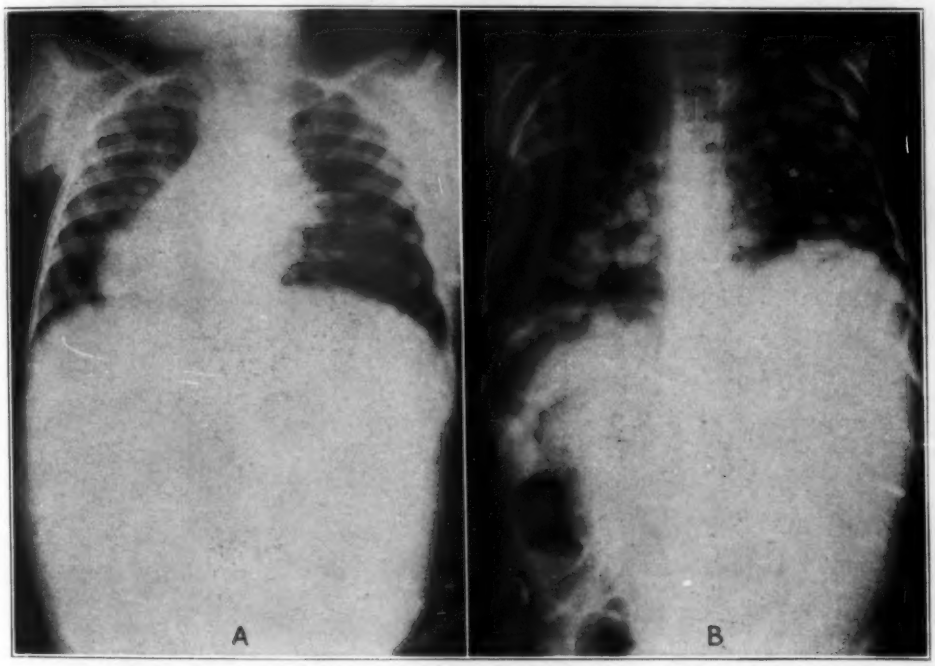

Fig. 11 (case 8).—*A*, sarcoma of the kidney with early metastases to the lungs. *B*, same as figure 11 *A* following the Coffey-Humber treatment, showing extensive and advanced metastases to both lungs.

The patient was given several roentgen treatments; the mass was reduced somewhat in size, and the hematuria had ceased. The parents were advised as to the gravity of the case, and decided to take the child to San Francisco for the Coffey-Humber serum treatment (Feb. 14, 1930). They remained in San Francisco three weeks, during which time he received six treatments. He had a violent reaction following the second injection, and was very ill for several days. The tumor grew rapidly, and the patient was much worse after the treatments; in fact, the parents were advised that he could live only a few days. Against the doctor's advice, he was brought home. Later he improved, and is again being treated by roentgen irradiation. On April 16, 1930, marked dyspnea developed, and a roentgenogram showed widespread involvement of both lungs. Eight treatments have

been given, with marked relief from the dyspnea and reduction in the size of the tumor. It is expected that the irradiation is only palliative.

A diagnosis of sarcoma of the right kidney with metastasis to both lungs was made.

CASE 9.—Mrs. C. D., aged 38, married, was admitted to the Steiner Clinic on April 20, 1927, complaining of intermenstrual bleeding, profuse menstrual periods and weakness. The present illness began four months before admission, when the patient noticed a slight bloody discharge or "spots" between periods, and recently her periods had been more profuse than usual. She had been growing weaker gradually for several months.

Examination of the chest gave negative results at the time of admission. The cervix was enlarged, with bilateral lacerations, and was eroded. It bled

Fig. 12 (case 9).—Secondary carcinoma of the lungs metastasized from the cervix uteri.

easily (apparently malignant). Otherwise physical examination gave negative results. A section from the cervix showed epidermoid carcinoma of the squamous type. A roentgenogram of the chest on April 20, 1928, showed metastatic carcinoma of the upper and outer portion of the left lung and also in the base of the right lung. On April 22, 1927, the red blood count was 4,000,000, with 75 per cent hemoglobin. On April 25, 1928, the red blood count was 2,800,000, with 40 per cent hemoglobin.

A final diagnosis was made of carcinoma of the cervix with secondary metastases to the lungs.

Radium was applied to the cervix, and roentgen therapy to the pelvic region in April and May, 1927.

On April 20, 1928, the cervix had healed entirely. The patient has symptoms of pulmonary complications, and the roentgenogram showed metastatic carcinoma,

which was unusual, with a primary lesion situated in the cervix uteri. In May, 1928, roentgen irradiation of the chest was instituted. The patient died on May 20, 1928.

Autopsy showed metastatic epidermoid carcinoma and bronchial pneumonia.

CASE 10.—Miss E. J., aged 27(?), was admitted to the Steiner Clinic on Aug. 7, 1925, complaining of sore throat, swelling on the left side of the neck, difficulty in swallowing and pain in the left ear. The present symptoms began about two months before admission, and had been progressive.

Examination revealed a moderate swelling on the left side of the neck, due to an enlargement of the cervical glands. A roentgenogram on August 7 showed in the third interspace on the right side an area of increased density, which was homogeneous, had smooth edges and extended from the mediastinal space half way to the periphery of the lungs.

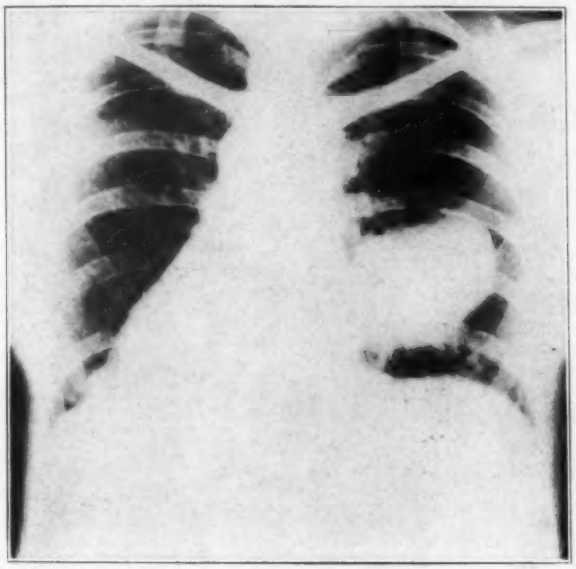

Fig. 13 (case 10).—Endothelioma of the lymph nodes with metastases to the lung.

The diagnostic impression was probably lymphosarcoma(?).

On August 8, biopsy of a lymph node, removed from the neck under procaine hydrochloride, showed endothelioma of the lymph nodes.

A final diagnosis was made of endothelioma of the lymph nodes with secondary metastases to the lungs.

Roentgen irradiation was employed on August 12, October 9, 12, 22 and 26. A roentgenogram on October 5 showed that the area had materially increased in size and that there was a new area just outside the heart shadow in the base of the left lung.

According to follow-up notes made on Nov. 4, 1925, the patient had been noncooperative from the beginning, had visited all the quacks and had not kept her appointments. She had a slight hemoptysis for two nights, decided that she had pulmonary tuberculosis and left for Los Angeles. The results are unknown.

CASE 11.—R. L., a Negro, aged 70, was admitted to the Steiner Clinic in August, 1925, complaining of a mass in the left side of the neck, enlarged glands of both the axillae and groins and dyspnea and cough. The present illness began in April, 1925, when the patient noticed a small lump on the left side of the neck which was not painful. Later other lumps appeared in the groins and axillae. The original growth progressed.

Examination showed a huge mass of enlarged glands on the left side under the ear, 10 by 8 by 6 cm. The tumor was firm and smooth; it was not attached to the skin, and was not tender. There were several smaller nodes on both sides of the neck which were freely movable. There was marked dulness in the apex of the right lung, sounds were normal, and no râles were present. There were enlarged glands in both axillae, not attached to the skin, and freely movable. Several enlarged, freely movable glands were found in each groin. A roentgeno-

Fig. 14 (case 11).—Hodgkin's disease.

gram of the chest on August 19 showed the right apex to be filled with dense shadows.

The diagnostic impression was (1) Hodgkin's disease and (2) lymphosarcoma.

In August, 1925, a small node was removed from the groin for diagnosis. A diagnosis of Hodgkin's disease was made.

Roentgen irradiation was given, with some improvement. The patient died in the summer of 1926 with acute diarrhea.

CASE 12.—Henry A. F. S., white, was admitted to the Steiner Clinic on Feb. 18, 1928, complaining of loss in weight, lumps under the arm and in the neck, weakness and loss of appetite. The present illness began when the patient "caught cold" in September, 1927. He later noticed the appearance of the masses in the arm pits and neck, and gradual loss in weight, weakness and lack of appetite.

Examination revealed that the glands of the neck were markedly enlarged and matted together, but were not sensitive to palpation. The glands of both axillae were enlarged. There was increased dulness on either side of the mediastinum,

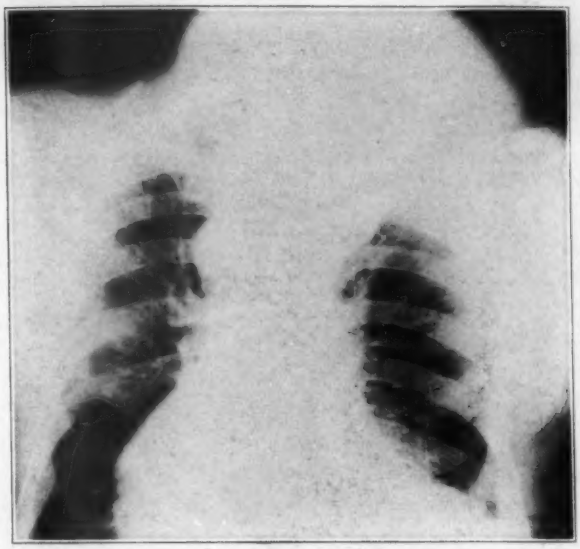

Fig. 15 (case 11).—Same as figure 14, showing involvement of the mediastinal glands.

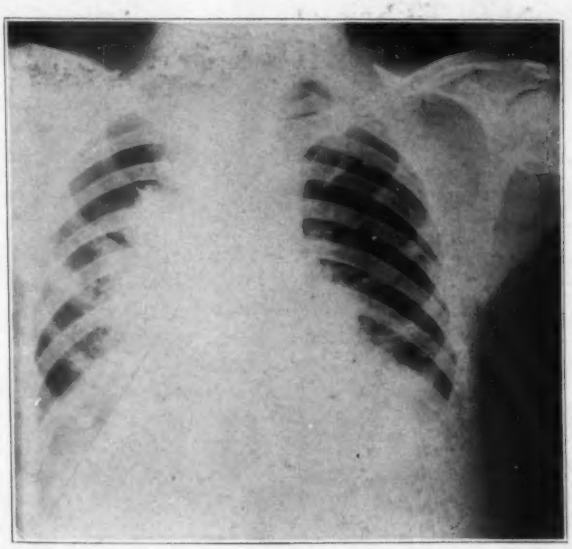

Fig. 16 (case 12).—Hodgkin's sarcoma with metastases to the lungs.

with a few scattering râles. Roentgenograms showed widespread involvement on either side of the sternum, extending well out to the periphery of both lungs at the bases.

The diagnostic impression was (1) lymphosarcoma and (2) Hodgkin's sarcoma. A gland was removed from the neck and a microscopic examination made. A diagnosis of Hodgkin's sarcoma with metastases to the lungs was made.

Roentgen treatment was given, with material reduction in the size of the masses. The patient died on April 22, 1928. Autopsy showed widespread Hodgkin's sarcoma throughout both lungs.

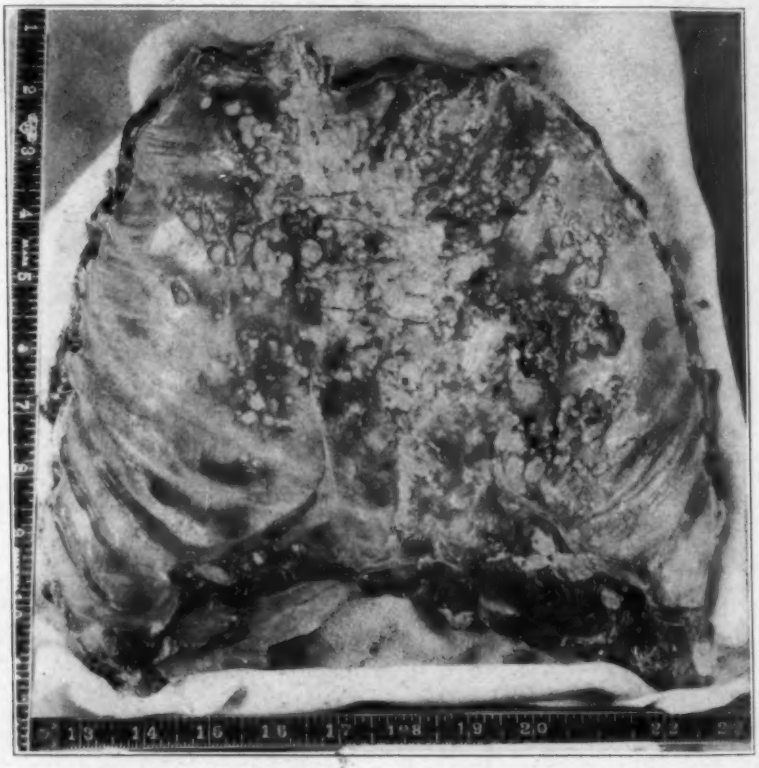

Fig. 17 (case 12).—Same as figure 16, showing autopsy specimen of the lungs.

Hodgkin's disease affects only the lymph tissues, whereas Hodgkin's sarcoma may metastasize like carcinoma or sarcoma; in this case it metastasized to the lungs.

Case 13.—Mrs. M. C. W., aged 69, was admitted to the Steiner Clinic on Jan. 23, 1929, complaining of several pigmented masses on the right side of the face, general weakness and loss in weight. The present illness had begun when the patient noted a small black wart or mole on the right eyebrow, which was removed in 1926 with a salve. The physician told her the growth was a cancer. It returned later and was not benefited by the application of salve or plaster. Later another mass appeared just anterior to the right ear, extending down on the neck. The cervical glands became enlarged. The hemoglobin was 80 per

Fig. 18 (case 13).—Melanoma of the face with metastases to both lungs.

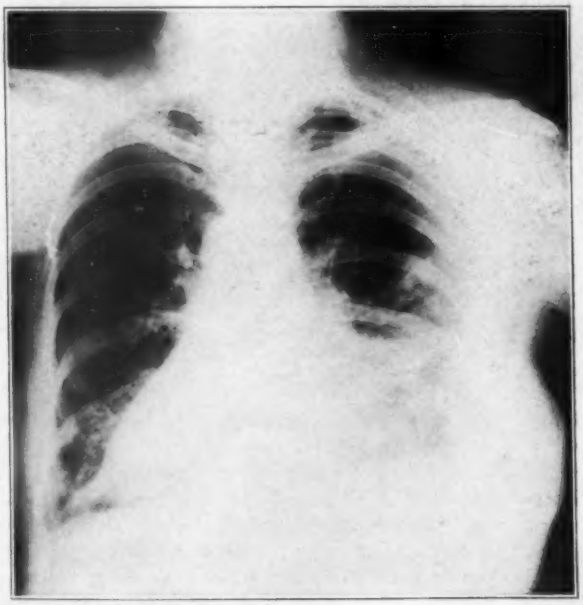

Fig. 19 (case 14).—Recurrent carcinoma of the left breast with extension to the pleura and lungs.

cent. The urine was positive for melanin. A roentgenogram of the chest showed widespread blood-borne metastases to both lungs.

A diagnosis was made of melanoma of the face (malignant) with metastases to both lungs.

Roentgen irradiation was given on January 26, 28 and 30 and February 28.

The patient died on March 17, 1929. Autopsy on March 18 showed metastases to the lungs, liver and spleen.

CASE 14.—Miss E. M. R., aged 43, was admitted to the Steiner Clinic on Jan. 13, 1927, complaining of an ulcerating mass on the anterior, left side of

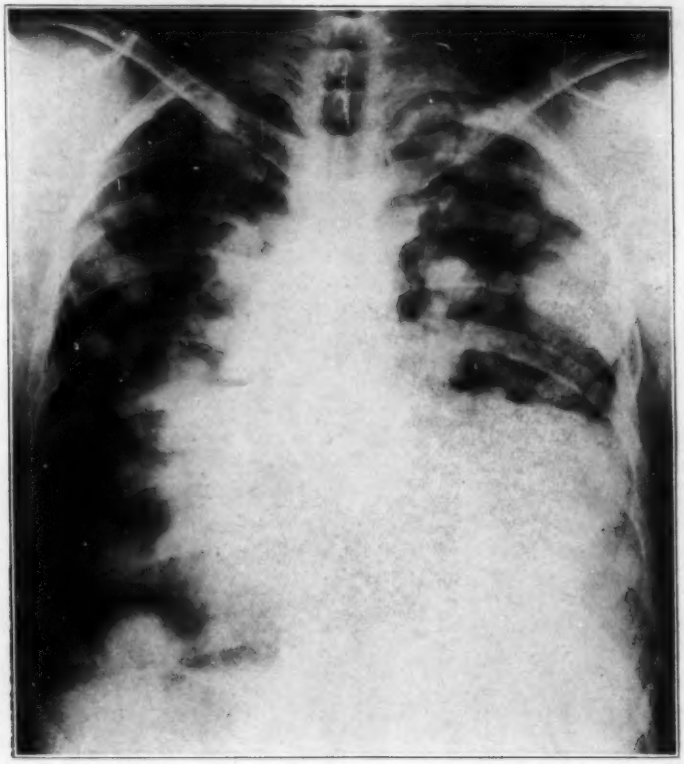

Fig. 20 (case 15).—Secondary carcinoma of the lungs from a malignant teratoma of the right testicle.

the thoracic wall. The present illness followed an automobile accident in October, 1925, in which the patient's left breast was bruised. A mass was noticed in December, 1925. She consulted a physician and was advised "to forget it." In October, 1926, the mass in the left breast was diagnosed as carcinoma. At this time small glands were palpable in the supraclavicular space. The breast was amputated. Roentgen therapy was given both before and after operation.

A roentgenogram on June 29, 1927, showed no evidence of thoracic metastases. On December 30, a roentgenogram showed involvement of the intrathoracic structures, probably a direct extension from the local recurrence rather than a metastasis.

A diagnosis was made of recurrent carcinoma of the left breast with direct extension to the pleura and possibly to the base of the left lung.

The patient died on March 25, 1928.

CASE 15.—J. L. L., aged 45, was admitted to my service at the Georgia Baptist Hospital on March 13, 1929, complaining of pains below the shoulder blade. The present illness began about three years before with swelling in the right testicle, with some edema of the scrotum. At first there was no pain; later sharp, darting pains developed. Six months before, the mass was removed and sent to the laboratory for diagnosis. The report showed teratoid tumor, suggestive of malignancy. A few weeks following operation, a mass developed in the right inguinal region and grew rapidly. Shortly afterward the patient noticed some difficulty in breathing, a feeling of fulness in the abdomen, some nausea and occasional vomiting. More recently, sharp pains had developed beneath the shoulder blades, and in the past month blood-tinged sputum, some cough and frequent night sweats had been noticed.

Examination revealed a poorly developed and emaciated man. The right side of the chest was more prominent than the left, with slight lagging on the left side on inspiration. Respirations were rapid, and breath sounds were harsh and wheezy. There was a hyperresonance anteriorly in both apexes, while posteriorly the resonance was impaired, and there was almost complete dulness. Moist râles were heard over the entire chest. The liver was enlarged and the spleen palpable. There was a tumor-like mass the size of an orange in the right inguinal region, and the scrotum contained a large mass on the right side. The Wassermann reaction of the blood was 4 plus. The patient was mildly anemic. A roentgenogram showed multiple round opaque shadows varying in size from 1 to 6 cm. in diameter throughout both lungs. There was a uniform dense shadow in the base of the right lung. A gland was removed from the groin. Microscopic examination showed teratoid tumor with carcinomatous changes.

A diagnosis was made of teratoid tumor of the right testicle, malignant, with carcinomatous metastases throughout both lungs.

The patient died on March 20, 1929. Autopsy confirmed the diagnosis.

CONCLUSIONS

Intrathoracic tumors, both benign and malignant, are more common than was formerly supposed.

Benign tumors of the mediastinum and lungs often produce atelectasis and bronchiectasis by pressure.

Primary carcinoma of the lung and pulmonary tuberculosis may coexist in the same patient.

Abscess and primary carcinoma of the lung often coexist, and it is impossible to tell which is cause and which is effect.

Benign tumors of the chest should be removed surgically when accessible.

Roentgen therapy offers only palliative results in malignant neoplasms within the chest.

Early surgical intervention is the only hope for primary malignant growths within the chest.

In the treatment for intrathoracic neoplasms, there should be a closer cooperation between the internist and the surgeon.

ABSTRACT OF DISCUSSION

DR. CARL A. HEDBLOM, Chicago: I quite agree with Dr. Lilienthal that "benign" is not a good term for nonmalignant tumor, but if such a tumor injures health or shortens life, as it frequently does, the term nonmalignant seems to me preferable to "benign" or "innocent."

I should like to emphasize the importance of the early recognition of tumors of the lung and of the thoracic wall. As Dr. Lilienthal so well stressed in his presidential address in 1923, any advance in treatment under present methods is dependent on early diagnosis.

We all agree, I think, that bronchoscopy is the most direct and the surest method of establishing the presence of bronchogenic tumor, but the diagnosis may be made not infrequently on biopsy of a hard cervical gland or of other superficial glands or tumors. Occasionally clumps of malignant cells may be isolated from the sputum or from aspirated pleural exudate.

In my opinion we should discriminate sharply between primary malignant tumors of the lung or the thoracic wall and those due to metastasis. Metastasis are common, as we all recognize, and signify, generally speaking, the same hopeless prognosis as metastasis elsewhere.

I have performed exploratory thoracotomies on a number of patients with bronchogenic carcinoma, but in every case the tumor had infiltrated the hilus. Radium implants in such cases in my experience seemed to prolong life and to relieve symptoms. I have drained abscesses secondary to tumor of the lung with marked palliative results. In cases with marked retraction of the mediastinum from atelectasis secondary to occlusions of the bronchus by the malignant growth, phrenicectomy may give some relief of the symptoms. In cases of indefinite tumors of the wall of the chest, early radical excision may be more conservative than waiting for a tumor to grow to such proportions that diagnosis becomes obvious but excision difficult or useless.

DR. WILLIAM A. HUDSON, Detroit: There is just one point in regard to the question of early diagnosis which I think cannot be emphasized too strongly. It has occurred to us that the developmental period of tumors of the lung is much longer than we have heretofore considered. We have now one case that has been under observation by numerous medical men over a period of seven years in which there was one symptom that was outstanding, and it was only after investigation of that particular symptom that a diagnosis was made. That symptom was spitting of blood. It recurred at irregular intervals throughout the period of observation. Bronchoscopy was performed on this patient three years ago by ourselves, at which time an ulcerative lesion was found in the lower lobe of the left bronchus; the lesion was not characteristically cancerous, but was suggestive. The patient was told at the time that it was a suspicious lesion, and that it should be kept under close observation. One year later bronchoscopy was performed by Dr. Clerf, who removed a specimen, and at the same time he told the patient that it was a suspicious lesion, but the specimen which was removed was reported as granulation tissue. Six weeks later we again performed a bronchoscopy and were able to penetrate to the orifice of a tertiary bronchus from which a nodule was seen to protrude. We removed a specimen smaller than my small finger-nail, removing practically the entire mass. Microscopic studies confirmed the suspicion of carcinoma of the bronchus. The patient has received radium and roentgen therapy and is still in good condition.

We feel that the developmental period is much longer than we have heretofore considered, this case presenting symptoms extending over a period of seven

years. Is it not possible that the development of the tumors such as Dr. Davison has shown extend over a period of ten, fifteen or even twenty years?

DR. L. T. LEWALD, New York: On account of the difficulty of making a differential diagnosis of some of the mediastinal tumors, I will show two slides to illustrate it. (For a report and illustration of this case see Roentgenologic Diagnosis of Thoracic Dermoids, ARCH. SURG. **18**:301 [Jan.] 1929.)

The tumor shown in the first slide occurred in a man, aged 37, and was said to have given slight pressure symptoms and slight dyspnea. The question of whether it was an aneurysm or a mediastinal dermoid is the point that I wish to emphasize. In regard to the question of pulsation, do not be misled by an apparent pulsation under the fluoroscope indicative of aneurysm. A tumor of this sort so closely related to the aorta and the heart will be lifted in such a way that one might believe that it showed pulsation. This tumor was examined by a number of roentgenologists, some of whom thought they saw pulsation. I first saw the case at the New York University Clinic, and diagnosed it as mediastinal dermoid, having seen one other case of mediastinal dermoid in which the patient was afterward successfully operated on by Dr. Lilienthal (ARCH. SURG. **18**:303 [Jan.] 1929).

The patient in question spontaneously coughed up the tumor. It is rather interesting that in a similar case, shown by Dr. Barker at the New York Academy of Medicine, a roentgenologist had diagnosed aneurysm and then showed a film like the second one presented, showing that the aneurysm had disappeared. The same thing happened in this case. Dr. Samuel Lambert obtained the final roentgenogram of this case for me at the Presbyterian Hospital two and a half years later. The patient entered the hospital at that time because of foul expectoration, and a roentgenogram made at that time showed that the tumor had disappeared, except for the sort of encapsulated appearance shown in the second slide. Dr. Lambert tried to trace the microscopic examination of the material that was coughed up, but was unable to find a report in the laboratory. His remark is that as the material was probably foul, and possibly contained hair, it was thrown away as not being a satisfactory specimen. He reports it in his article on intrathoracic tumors as a mediastinal dermoid that suppurated and was evacuated in this way.

DR. HOWARD LILIENTHAL, New York: I have often wondered about the mistaking of dermoids and tumors of that sort for aneurysms on account of the apparent expansile pulsation. There may be an excuse for such mistakes.

We do not look at the tumor merely on a plane, it is not merely pushed to the side by the heart; it may be pushed away from the observer and, therefore, become larger in all dimensions as it goes away from him and smaller in all dimensions as it approaches him, thus simulating a true expansile pulsation. I should like to know what Dr. LeWald thinks of this.

DR. L. T. LEWALD, New York: I think that this explanation sounds reasonable; however, I should like to see it proved in a series of rapidly made exposures in which one could study the phenomenon differentially rather than to trust to one's eye and the fluoroscope alone.

DR. T. C. DAVISON, Atlanta, Ga.: It is hoped that an abstract of this discussion may be placed before the medical profession in order to stimulate increased interest in intrathoracic tumors, and to bring about a closer cooperation between the internist and the surgeon.

REMOVAL OF METASTATIC CARCINOMA OF THE LUNG AND MEDIASTINUM

SUGGESTIONS AS TO TECHNIC

FRANZ TOREK, M.D.
NEW YORK

History.—Mrs. C. T., aged 42, had had a complete hysterectomy for carcinoma, performed by Dr. Arthur Stein in May, 1927. The recovery was normal in all respects, except that a vesicovaginal fistula ensued. This was operated on by Dr. Stein in August, 1927, and healed.

The patient remained well until August, 1929, when she began to complain of dysphagia, which by November became so much worse that she was no longer able to eat solid food. Her weight dropped from 105 pounds (47.6 Kg.) in August to 90 pounds (40.8 Kg.) in December. There was no history of pulmonary disease, no cough or pain in the chest. Occasionally, she felt her heart pound somewhat.

Roentgen examination on December 26 revealed a large, smooth, round, sharply circumscribed mass in the right portion of the chest, extending beyond the right border of the heart. It occupied the area of the eighth, ninth and tenth intercostal spaces and measured about 11 cm. across. The lower half of the esophagus was displaced forward by the mass, being sharply angulated where it came in contact with the upper border of the tumor. At the diaphragm the tumor was pressed against the anterior part of the hiatus. The heart was also pressed forward. The stomach was ptosed; it showed a large six hour retention and a small twenty-four hour residue. The descending duodenum was the seat of a diverticulum. A vaginal and abdominal examination, made by Dr. Stein, showed no local recurrence.

I saw the patient early in January, 1930. An examination revealed dulness low down on the posterior aspect of the chest, especially on the right side; on the left side there was also dulness, but here it was confined to an area close to the spine. The breath sounds over the dull area were faint; above that area the voice transmission was exaggerated. An occasional râle was heard here and there.

The patient's history pointed strongly toward the diagnosis of metastatic carcinoma of the lung. However, the outline of the new growth was so well defined that the roentgenologists as well as the physicians, including myself, considered the roentgen picture to be characteristic of a nonmalignant growth, probably a mediastinal dermoid. As is usual with dermoids in that location, the esophagus and the heart also, to some extent, had been displaced forward. This diagnosis seemed to be further supported by the fact that the gynecologist could find nothing suggestive of a local recurrence. Finally, there seemed to be no good reason for assuming that a patient who had had carcinoma should not also have a mediastinal dermoid.

Attempts were made at the hospital to feed the patient previous to her operation; but instead of gaining, she even lost weight during the attempt.

Operation.—Operation was performed on January 20. I had planned to remove the supposed mediastinal dermoid extrapleurally, if possible. A posterolateral incision was made through the eighth intercostal space from the angle of the

rib to the midaxillary line, and a second incision was made from the posterior end of the first incision downward, corresponding to the ninth, tenth and eleventh ribs. The incision was carried down to the pleura but not through it. The parietal pleura was separated from the eighth and ninth ribs, well forward beyond the anterior end of the incision and well backward to the spine. Then it was loosened down to the diaphragm. In the course of this procedure, the ninth, tenth and eleventh ribs were cut about at their angles, as soon as each one had been separated from its parietal pleura. It soon became apparent that the mass was a tumor of the lung which had extended into the mediastinum and had become firmly attached to its surroundings, especially at the diaphragm and the vertebrae. The dissection was nevertheless continued extrapleurally, since thus the likelihood of remaining outside the involved area was enhanced and the lung could retain its normal covering of parietal pleura for a maximum amount of

Fig. 1.—Tumor of the lung and mediastinum. The tumor occupies an area from the eighth to the tenth intercostal space inclusive and measures 11 cm. across. It is for the most part on the right side and has pushed the esophagus forward, causing obstruction which is most marked at the hiatus, where the esophagus could not yield so well to the pressure of the tumor.

time. Finally, the last step in the resection, that of cutting the tumor off the lung and of properly caring for the cut surface, could be done best when the new growth required no further care and when the operator's attention could be centered on the only surface from which bleeding was still to be expected. There was some spurting from the cut surface of the lung, which was caught without much difficulty, and the raw surface was later closed by a continuous catgut suture. The pleura was then sutured whever possible, but this could be done only partially, because portions of it had to be sacrificed in the removal. The lung was then inflated, and the wound closed without drainage, using two pericostal sutures of chromic catgut to approximate the eighth and ninth ribs, chromic gut for the muscles and silk for the skin. After the patient had been brought back to her room, she was given a blood transfusion of 500 cc.

Course.—The wound healed without any disturbance. As I was uncertain whether the wound in the lung had been closed air tight, frequent examination was made the first few days for the presence of a mediastinal emphysema, but none occurred. A pleuritic exudate of moderate extent, on the right side, which gave rise to no subjective symptoms, was noted after the operation and had not been completely reabsorbed after six weeks. It has since disappeared. A roentgenogram taken about that time showed the absence of the tumor. The esophagus was more nearly straight but not properly filled, which latter condition was believed to be ascribable partly to adhesions, partly to spasm invoked reflexly by

Fig. 2.—The patient after the wound had healed, showing the incision which goes through the eighth intercostal space, with an extension from its mesial end downward over three ribs which were divided.

the duodenal diverticulum with the twenty-four hour residue in the stomach. At any rate, the patient had for some time been able to eat meat, vegetables, bread, etc., provided she ate slowly.

Pathologic Report.—The tumor was composed of a thin, interlacing stroma in which was soft, friable, almost gelatinous tissue. The tumor was vascular, and several areas of diffuse hemorrhage were seen in its substance. Sections of the peripheral portions showed a carcinoma composed, for the most part, of columns and islands of pavement epithelium supported by delicate strands of fibrous tissue bearing this epithelium with blood vessels of small caliber. The greater part of

Fig. 3.—The tumor.

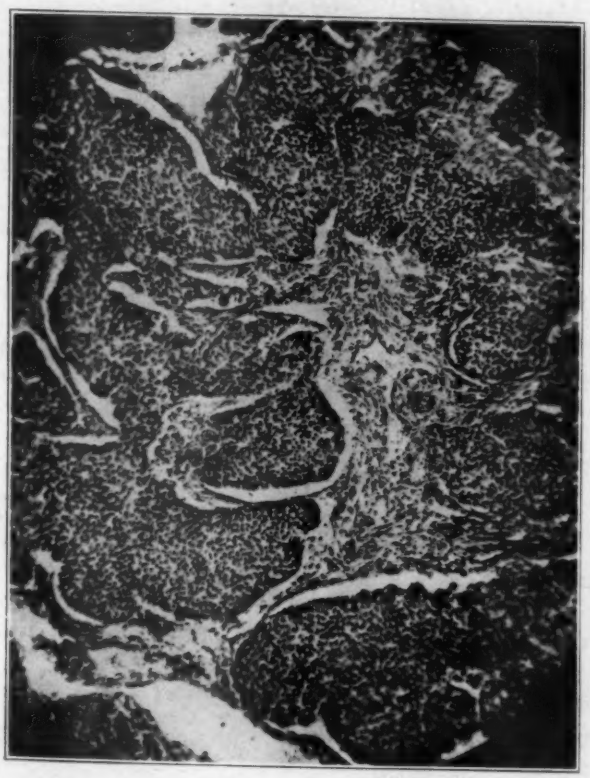

Fig. 4.—Photomicrograph of the adeno-acanthoma.

the epithelium showed neither intercellular bridges nor epithelial pearls. The constituent cells were usually small and hyperchromatic, though there were areas composed of larger cells which stained less deeply with hematoxylin. Mitotic figures were fairly numerous. In many areas there were small masses of nests of differentiated squamous epithelium often showing central cornification or pearl formation. Included in the tumor were a few small spaces bordered by cylindric epithelium or more or less well defined glandular acini. Near one surface of the tumor there were small islands of pulmonary tissue, and attached to the surface was a small amount of atelectatic lung tissue. Toward the deepest part, the tumor showed extensive necrosis, sometimes with replacement fibrosis. In the newly formed fibrous tissue were a number of cholesterol crystal spaces, often bordered by giant cells. A diagnosis of adeno-acanthoma of the lung and posterior mediastinum, secondary to adeno-acanthoma of the uterus was made.

Fig. 5.—Roentgenogram after removal of the tumor. The esophagus has straightened out considerably but is still somewhat out of shape, due probably to adhesions.

COMMENT

As the tumor was a metastatic one, this history is, of course, not presented as that of a case in which cure was obtained. Metastases are more likely to be multiple than solitary, and I saw some enlarged lymph nodes at the right bronchus but did not take any out for examination, as a prolongation of the operation did not seem warranted. There is, possibly, one brighter side to the case in the fact that uterine carcinomas are fairly radiosensitive and that this carcinoma of the lung is identical in type with the original uterine new growth. Working on this hypothesis, the patient has already received two series of deep roentgen treatments and is at the present time back in the hospital for a third series.

The case is of interest because it offers a few topics for consideration. In the first place, there is the question of the permissibility of operating at all in the case of a metastasis. Frankly, I must admit, that had I known positively that the tumor was a metastasis, I doubt that I would have had the courage to operate. I operated under a wrong diagnosis, with the rather unexpected result that the patient is thankful to me for doing so. Now, having had this experience, I should not be inclined to be too dogmatic in refusing to remove a metastatic new growth. In this case, the tumor caused obstruction of the esophagus, and that fact, I think, was sufficient reason for removing the tumor. One should, I believe, be guided by the indications in each case and not take a hard and fast stand for or against the removal of a metastatic new growth.

In the second place, the technic might deserve consideration, not simply in its application to this particular case, but also in its application to primary tumors of the lung. In some of these primary carcinomas, the extrapleural approach may perhaps be of advantage, provided the tumor is situated near a margin or corner of the lung. The customary attack is intrapleural, and in the course of it, one frequently encounters firm adhesions binding the affected lung to the parietal pleura. If the resection is made outside of these adhesions, extrapleurally, the likelihood that one is proceeding in unaffected tissue is greater than if these adhesions are divided intrapleurally.

In the third place, although even with an intrapleural approach it is feasible to excise the aforementioned adhesions of a carcinoma of the lung together with their parietal pleura, this extrapleural method has the additional advantage of permitting the lung to remain protected by the best possible covering, its own pleura, for a maximum length of time, thus reducing to a minimum the irritation of its surface, to which it would otherwise be subjected by pads, hands and other foreign material. Grave of Moscow claimed that irritation of the terminal sensory vagus filaments of the lung caused "vagus pulse" and disturbance of respiration. The retention of the parietal pleura as long as possible would undoubtedly reduce any possible vagus irritation from that source.

ABSTRACT OF DISCUSSION

DR. WILLY MEYER, New York: As far as therapy is concerned, bronchoscopy is a close running mate with surgery in many conditions of the lung. We have seen and heard again this morning—and we all know it from our own personal experience for years—that many bronchiectatic conditions and abscess of the lung can be cured by bronchoscopy and bronchoscopic treatment. If the bronchoscopist is strict in his self-criticism and after a certain time is ready to say, "I am at my wits' end, now this case will go to the surgeon," the patient will have been done full justice. The same can be said about other diseases of the lung. After all, the saving of life is the principal point in medical and surgical

treatment; we know that the danger from bronchoscopy and intrabronchial treatment is much less than that from an operation. If science can possibly help a patient with milder means, often permanently, this should be tried first.

Regarding cancer of the lung, we know that in at least 90 per cent of the cases the trouble starts in the main bronchus, principally in the right. What does such a patient show clinically, who is afflicted with a beginning cancer of the bronchus? He has principally the inclination to cough, a cough that cannot be explained, because no pathologic condition is found by the internist, and nothing is shown at that early time by roentgenographic examination. If the attending physician is progressive and properly trained, he will soon consider bronchoscopy, suspecting perhaps a malignant tumor in the bronchus, suspicion of the presence of a foreign body being unfounded. And if the specialist finds an irregularity of the surface of the bronchial mucosa, he will make a biopsy and let the pathologist tell him the diagnosis.

Regarding the value of a therapeutic proposition in medicine, I have always believed that if two minds have had the same idea about the treatment for some trouble, independently, there is likely something useful in what they are proposing. By chance, I read a paper before our Association on cancer of the lung two years ago. While working on it, I wondered whether one should not, if the condition were definitely diagnosed, attack that small, beginning tumor of the bronchus at once as radically as possible, namely, thoroughly burn it away with actual cautery. With this in mind, I went to the attending laryngologist and bronchoscopist of our hospital, Dr. John D. Kernan. I said to him, "Dr. Kernan, can you invent or construct an instrument which, introduced through the bronchoscope, will permit you to thoroughly cauterize that place in the wall of the bronchus, from where you took the biopsy, which permitted the pathologic diagnosis?"

He smiled and said, "Doctor, I have done that already."

A report of his case has not been published so far. The gist of the matter is that an early cancer definitely diagnosed by the pathologist from a biopsied specimen was thoroughly cauterized through the bronchoscopic tube, and was also treated later on with gold radon implants introduced and placed through the tube, and the patient, a woman, was cured, and was still cured when I last heard of her through Dr. Kernan a few days ago.

A second case, also that of a patient of Dr. Kernan, is on record. The fact is that Dr. Kernan had the primary idea, and that I had the same, independently. Such occurrence would have been some firm basis for action on these lines even if we were not yet in possession of two cases of early cancer in which cure appeared to be obtained in this way. Besides making the correct diagnosis, the point worth emphasizing is the actual cauterization. The more intensive the local reactive hyperemia produced, the greater is the hope for a radical cure.

Why is it that a cancer of the lung starts in the bronchus so frequently and not in the parenchyma? Because, we believe, the careful analysis of the development of cancer shows that a cancer, not only of the lung, but of any organ, develops with predilection in places generally where there is more rest, and in that part of the same organ which is least active. On the other hand, where there is much motion, viz., active hyperemia, i. e., strong circulation due to the activity of the organ, there occurs rarely, if at all, the formation of cancer.

A few years ago, at one of the annual meetings of the American Association for Cancer Research, a member, speaking of the subject of chronic irritation, said, "If one could but explain why the breast of a farmer's milk cow, that is

so battered and maltreated by the calf and not only by the calf but by the oldtime process of milking day after day, hardly ever becomes the seat of a cancer." A few years later, being engaged in studies on the genesis and on the development of cancer, I ventured to give the explanation just mentioned. The heart muscle, at work day and night, is very rarely the seat of primary cancer. We eat three times a day; six hours is the longest time the food stays in the stomach; from there it passes on at brief intervals into the duodenum stimulating it to almost continuous activity. With four large-sized arteries feeding the area with blood, the duodenum rarely harbors a cancer. Of course, we know that chemistry likely also plays a rôle in the etiology.

Coming back to the subject of cancer of the lung, I am absolutely convinced that if we all band together, at least the members of our Association, and impress on our confrères that a patient with a persistent unexplained cough must be given a bronchoscopic examination, and if the bronchoscopist takes a specimen by means of biopsy and the pathologist finds it malignant, with early removal with the wire sling, if pedunculated, and thorough cauterization with subsequent treatment along conservative lines, the terrible hardship for patients with cancer of the lung will gradually disappear and more cases of a permanent cure of cancer of the bronchus placed on record.

Years ago I had a patient with a large intrathoracic pulsating tumor; it made the entire chest pulsate and did not have the earmarks of a typical aneurysm. It was hard to explain. On exploratory thoracotomy, an enormous distention of the entire aorta, a massive total aortic aneurysm, was found. It began at the arch of the aorta and went down to the space where the vessel passes through the diaphragm. Nothing could be done surgically. I closed the thorax, and the patient recovered so far as the operation was concerned. The case proves, that even in such dangerous cases of pathologic processes, the body stands an exploratory thoracotomy very well. Today we know that exploratory thoracotomy is no more dangerous than exploratory laparotomy. Why then not, when one sees on the x-ray plate an intrathoracic tumor and the patient is suffering, make an exploratory thoracotomy and see whether we can bring help?

I wish to congratulate Dr. Torek that he went ahead in this case and had success.

Dr. Pol N. Coryllos, New York: I want to congratulate Dr. Torek on reporting his error in the diagnosis of the metastatic character of this tumor, which led him to such excellent operative success and gave us the opportunity to hear about this unusual case. It is the first case, to my knowledge, of an operation on a secondary carcinoma of the lung. This shows that in cases of metastatic tumor of the lung, complicated by compression of the intrathoracic organs endangering the life of the patient, a radical procedure is perfectly legitimate. It shows, furthermore, that the distinction between tumors of the lungs as benign, malignant or whatever else one may wish to call them has no practical significance. There is no such thing as a "benign" or even an "innocent" tumor of the lung or of the thoracic cavity, if such tumor is liable to increase in size. A time inevitably comes when by its mere growth it produces by compression complications jeopardizing the life of the paient. I should suggest to differentiate tumors by the terms "operable" and "inoperable," and to operate on them first and leave the laboratory to determine afterward their exact nature and grade of malignancy.

I am in perfect accord with the opinion of Dr. Torek concerning the great advantages of the extrapleural approach. Yet if the lung is free from adhesions,

I do not think there are many advantages in using this method. A preliminary, artificial pneumothorax, by allowing us to estimate the existence or absence of pleuropulmonary adhesions, would give some valuable indications as to the procedure to follow.

Another remarkable point in this case is the facility with which the tumor was enucleated. This shows once more that in thoracic surgery, especially for tumors of the lung, well measured boldness is of great value.

PROCEEDINGS

Sunday, May 11

The Council met in an executive session at 8 p. m.

Monday, May 12

A dry clinic was given by the staff at the Jefferson Hospital at 9 a. m.

The meeting convened at 2 p. m. at the College of Physicians, Mitchell Hall.

The following papers were read:

Dr. Edgar W. Phillips, Rochester, N. Y.: "Hydatid Cysts of the Lung: Review of the Recorded North American Cases."

Dr. Stuart W. Harrington, Rochester, Minn.: "Amebic Hepatic, Subphrenic and Pulmonary Abscesses."

Dr. Howard Lilienthal, New York: "Giant Sarcoma of the Pleura: Report of Two Cases with Remarks on Operative Exploration of the Thorax."

Dr. T. C. Davison, Atlanta, Ga.: "Intrathoracic Tumors: Report of Cases."

Dr. Franz Torek, New York: "Removal of Metastatic Carcinoma of the Lung and Mediastinum: Suggestions as to Technic."

Dr. Claude S. Beck and Dr. R. A. Griswold, Cleveland: "Pericardiectomy in the Treatment of the Pick Syndrome: Experimental and Clinical Observations."

Tuesday, May 13

Demonstrations of methods of the technic and of experimental work were given by the staff of the University Hospital at 9:30 a. m.

The Council met in executive session at 1 p. m.

The meeting convened at 2 p. m. at the College of Physicians, Mitchell Hall. The Association met in executive session for the election of officers, new members and such other business as was brought before the meeting.

The following papers were presented:

Dr. Wyman Whittemore, Boston: President's Address, "Exploration of the Pericardium and Decompression of the Heart: Report of Case."

Dr. Carl A. Hedblom, Chicago: "Anterolateral Costectomy for Inadequate Collapse Following Posterior Extrapleural Thoracoplasty."

Dr. Frank B. Berry, New York: "The Unfavorable Results of Phrenicectomy."

Dr. E. J. O'Brien, Detroit: "Collapse Therapy: Reasons for and Mechanisms of the Therapy with Deductions Based on Observations of Seven Hundred Patients."

Dr. Francis A. C. Scrimger, Montreal, Canada: "Idiopathic Dilatation of the Esophagus."

Dr. H. C. Ballon, Dr. H. M. Wilson (by invitation), Dr. J. J. Singer and Dr. E. A. Graham, St. Louis: "Esophagus, Stomach and Heart Following Unilateral Phrenicectomy."

Dr. Duff S. Allen, St. Louis: "The Treatment for Penetrating Wounds of the Pleural Cavity."

President's Banquet was held at the Mask and Wig Club, University of Pennsylvania at 7 p. m.

WEDNESDAY, MAY 14

The meeting convened at 9:30 a. m. at the College of Physicians, Mitchell Hall. The subject of promotion from active to senior membership was discussed.

The following papers were read:

Dr. David T. Smith, Ray Brook, N. Y.: "Etiology of Primary Bronchiectasis."

Dr. John H. Gibbon, Jr. (by invitation) and Dr. Edward D. Churchill, Boston: "Changes in the Pulmonary Circulation Induced by Experimentally Produced Arteriovenous Fistula."

Dr. C. M. Van Allen, Peiping, China, and Dr. G. E. Lindskog, New Haven, Conn.: "Obstructive Pulmonary Atelectasis: Problems of Pathogenesis and Clinical Management."

Dr. Pol N. Coryllos and Dr. George L. Birnbaum (by invitation), New York: "Atelectasis of the Lung: Rôle of Alveolar Gas Exchanges in Its Production."

REPORT ON THE ACTIVITIES OF THE CHEST TUMOR REGISTRY

During the past year, the recommendations of the Council of the Association relative to the preparation and circulation of special blanks for the registration of chest tumors have been carried out. Several hundred of these blanks have been sent out, and the response has been gratifying. At present, the Registry contains records of about 100 cases. We have also received replies to a circular letter sent to members of the Association which contain promises of submission of at least 50 additional cases.

The Registrar has answered numerous inquiries concerning the Registry from surgeons throughout the country who are not members of the American Association for Thoracic Surgery, and blanks have been sent out for the registration of their cases. In addition, we are corresponding with several foreign clinics and hope to be able to obtain records of a considerable number of chest tumors from them.

Respectfully submitted,

WILLIAM DEW. ANDRUS, Registrar.

CHANGES IN CONSTITUTION AND BY-LAWS

At the Thirteenth Annual Meeting of the American Association for Thoracic Surgery, Article VII, Section 7 of the By-Laws was amended to read as follows:

"In printing and publishing the annual transactions of the Association, it will incur expenses not to exceed $60 for each article. If the cost for printing and illustrating any article exceeds this sum, the excess shall be charged as a special assessment against the author concerned."

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